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(21) International Application Number: PCT/US99/07333 (22) International Filing Date: 2 April 1999 (02.04.99) (30) Priority Data: 60/080,671 3 April 1998 (03.04.98) US (71) Applicant (for all designated States except US): NPS PHARMACEUTICALS, INC. [US/US]; Suite 240, 420 Chipeta Way, Salt Lake City, UT 84108 (US). (72) Inventors; and (75) Inventors/Applicants (for US only): STORMANN, Thomas, M. [US/US]; 1327 E. Harrison, Salt lake City, UT 84105 (US). HAMMERLAND, Lance, G. [US/US]; 3201 South 400 East, Salt Lake City, UT 84010 (US). STORJOHANN, Laura, L. [US/US]; 2592 East Stanford, Salt Lake City, UT 84117 (US). BUSBY, James, G. [US/US]; 3256 East Del Verde, Salt Lake City, UT 84109 (US). GARRETT, James, E. [US/US]; 1584 East 3150 South, Salt Lake City, UT 84106 (US). SIMIN, Rachel, T. [US/US]; 1520 East Redondo Avenue, Salt Lake City, UT 84105 (US). (74) Agent: WARBURG, Richard, J.; Lyon & Lyon LLP, 4225 Executive Square, La Jolla, CA 92037 (US).	(81) Designated States: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, ARIPO patent (GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG). Published <i>With international search report.</i> <i>Before the expiration of the time limit for amending the claims and to be republished in the event of the receipt of amendments.</i>	
(54) Title: G-PROTEIN FUSION RECEPTORS AND CHIMERIC GABA _B RECEPTORS (57) Abstract The present invention features G-protein fusion receptors and chimeric GABA _B receptors (GABA _B Rs), nucleic acid encoding such receptors, and the use of such receptors and nucleic acid. G-protein fusion receptors comprise at least one domain from a CaR, a mGluR, and/or a GABA _B receptor fused directly or through a linker to a guanine nucleotide-binding protein (G-protein). Chimeric GABA _B Rs comprise at least one of a GABA _B R extracellular domain, a GABA _B R transmembrane domain, or a GABA _B R intracellular domain and one or more domains from a mGluR subtype 8 (mGluR8) and/or a CaR.		

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Exhibit 6

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DESCRIPTIONG-PROTEIN FUSION RECEPTORS AND CHIMERIC GABA_A RECEPTORSRELATED APPLICATIONS

5 The present application claims priority to Garrett et al. U.S. Serial No. 60/080,671, filed April 3, 1998, which is hereby incorporated by reference herein in its entirety including the drawings.

FIELD OF THE INVENTION

10 The present invention relates to a G-protein fusion receptors, chimeric GABA_A (γ-aminobutyric acid) receptors, nucleic acid encoding such receptors, and uses of such
15 receptors and nucleic acid encoding such receptors.

BACKGROUND

The references cited herein are not admitted to be prior art to the claimed invention.

20 Chimeric receptors made up of peptide segments from different receptors have different uses such as being used to assess the functions of different sequence regions and to assess the activity of different compounds at a particular receptor. Examples of using chimeric receptors to assess the activity of
25 different compounds are provided by Dull et al., U.S. Patent No. 4,859,609, Dull et al., U.S. Patent No. 5,030,576, and Fuller et al., International Application No. PCT/US96/12336, International Publication No. WO 97/05252.

Dull et al. U.S. Patent No. 4,859,609, and Dull et al. U.S.
30 Patent No. 5,030,576, indicate the production and use of chimeric receptors comprising a ligand binding domain of a predetermined receptor and a heterologous reporter polypeptide. The Dull et al. patents provide as examples of chimerics: (1) a chimeric
35 receptor made up of the insulin receptor extracellular α chain, and the EGF receptor transmembrane and cytoplasmic domains without any HIR B-chain sequence; and (2) a hybrid receptor made

up of the v-erbB oncogene product intracellular domain fused to the EGF receptor extracellular and transmembrane domains.

Fuller et al. International Publication No. WO 97/05252 feature chimeric receptors made up of metabotropic glutamate receptor (mGluR) domains and calcium receptor (CaR) domains. The chimeric receptors allow the coupling of functional aspects of a mGluR with a CaR.

An example of the use of chimeric receptors to assess the functions of different sequence regions receptors are found in studies identifying regions of different guanine nucleotide-binding protein coupled receptors important for guanine nucleotide-binding protein coupling. (See, Kobilka et al., *Science* 240:1310-1316, 1988; Wess et al., *FEBS Lett.* 258:133-136, 1989; Cotecchia et al., *Proc. Natl. Acad. Sci. USA* 87:2896-2900, 1990; Lechleiter et al., *EMBO J.* 9:4381-4390, 1990; Wess et al., *Mol. Pharmacol.* 38:517-523, 1990; and Pin et al., *EMBO J.* 13:342-348, 1994.)

SUMMARY OF THE INVENTION

The present invention features G-protein fusion receptors and chimeric GABA_B receptors (GABA_BRs), nucleic acid encoding such receptors, and the use of such receptors and nucleic acid. G-protein fusion receptors comprise at least one domain from a CaR, a mGluR, and/or a GABA_B receptor fused directly or through a linker to a guanine nucleotide-binding protein (G-protein). Chimeric GABA_BRs comprise at least one of a GABA_BR extracellular domain, a GABA_BR transmembrane domain, or a GABA_BR intracellular domain and one or more domains from a mGluR subtype 8 (mGluR8) and/or a CaR.

G-proteins are peripheral membrane proteins made up of an α subunit, a β subunit, and a γ subunit. G-proteins interconvert between a GDP bound and a GTP bound form. Different types of G-proteins can affect different enzymes, such as adenylate cyclase and phospholipase-C.

Thus, a first aspect of the present invention describes a G-protein fusion receptor comprising:

an extracellular domain comprising an extracellular domain amino acid sequence substantially similar to either an extracellular CaR amino acid sequence, an extracellular mGluR amino acid sequence, or an extracellular GABA_A receptor amino acid sequence;

5 a transmembrane domain joined to the carboxy terminus of said extracellular domain, said transmembrane domain comprising a transmembrane domain amino acid sequence substantially similar to either a transmembrane CaR amino acid sequence, a transmembrane mGluR amino acid sequence, or a transmembrane GABA_A receptor amino acid sequence;

10 an intracellular domain joined to the carboxy terminus of said transmembrane domain comprising all or a portion of an intracellular amino acid sequence substantially similar to either an intracellular CaR amino acid sequence, an intracellular mGluR amino acid sequence, or an intracellular GABA_A receptor amino acid sequence, provided that said portion is at least about 10 amino acids;

an optionally present linker joined to the carboxy terminus of said intracellular domain; and

20 a G-protein joined either to said intracellular domain or to said optionally present linker, provided that said G-protein is joined to said optionally present linker when said optionally present linker is present.

25 "Substantially similar" refers to at least 40% sequence similarity between respective polypeptide regions making up a domain. In preferred embodiments, substantially similar refers to at least 50%, at least 75%, at least 90%, at least 95% sequence similarity, or 100% (the same sequence), between polypeptide domains. The degree to which two polypeptide domains are substantially similar is determined by comparing the amino acid sequences located in corresponding domains. Sequence similarity is preferably determined using BLASTN (Altschul et al., *J. Mol. Biol.* 215:403-410, 1990).

30 The different receptor components of the G-protein receptor can come from the same receptor protein or from a chimeric receptor made up of different receptor domains. By swapping different domains compounds able to effect different domains of a

particular receptor can be identified and the activity of different compounds at different domains can be measured.

In different embodiments the CaR region(s) present in the G-protein fusion are substantially similar to, comprise, or consist of portion(s) of the human CaR; mGluR region(s) present in the G-protein fusion are substantially similar to, comprise, or consist of portion(s) of a human mGluR; and GABA_BR region(s) present in the G-protein fusion are substantially similar to, comprise, or consist of portion(s) of a human GABA_BR receptor.

In preferred embodiments concerning GABA_BR regions that are present: the GABA_BR extracellular domain is substantially similar to a GABA_BR extracellular domain provided in SEQ. ID. NOS. 2-4; the GABA_BR transmembrane domain is substantially similar to the GABA_BR transmembrane domain provided in SEQ. ID. NOS. 7-9; and the GABA_BR intracellular domain is substantially similar to a GABA_BR intracellular domain provided in SEQ. ID. NOS. 12-14.

In preferred embodiments concerning CaR regions that are present: the CaR extracellular domain is substantially similar to the CaR extracellular provided in SEQ. ID. NO. 1; the CaR transmembrane domain is substantially similar to the CaR transmembrane domain provided in SEQ. ID. NO. 6; and the CaR intracellular domain is substantially similar to the CaR intracellular domain such as that provided in SEQ. ID. NO. 11.

Various different mGluR subtypes present in different organisms, including humans, are described in different patent publications as follows: mGluR₁ - WO 94/29449, EP 569 240 A1, WO 92/10583 and U.S. Patent No. 5,385,831; mGluR₂ - WO 94/29449, WO 96/06167, and EP 711 832 A2; mGluR₃ - WO 94/29449, and WO 95/22609; mGluR₄ - WO 95/08627, WO 95/22609, and WO 96/29404; mGluR₅ - WO 94/29449; mGluR₆ - WO 95/08627; mGluR₇ - U.S. Patent No. 5,831,047, WO 95/08627 and WO 96/29404; and mGluR₈ - WO 97/48724 and EP 816 498 A2. (Each of these references are hereby incorporated by reference herein.)

In preferred embodiments concerning mGluR regions that are present: the mGluR extracellular domain is substantially similar to either human mGluR 1, human mGluR 2, human mGluR 3, human mGluR 4, human mGluR 5, human mGluR 6, human mGluR 7, or human

mGluR 8; the mGluR transmembrane domain is substantially similar to either human mGluR 1, human mGluR 2, human mGluR 3, human mGluR 4, human mGluR 5, human mGluR 6, human mGluR 7, or human mGluR 8; and the mGluR intracellular domain is substantially similar to either human mGluR 1, human mGluR 2, human mGluR 3, human mGluR 4, human mGluR 5, human mGluR 6, human mGluR 7, or human mGluR 8.

Another aspect of the present invention describes a nucleic acid comprising a nucleotide sequence encoding for a G-protein fusion receptor.

Another aspect of the present invention describes a recombinant cell comprising an expression vector encoding for a G-protein fusion receptor, and a cell where the G-protein fusion receptor is expressed. Preferably, the G-protein fusion receptor is functional in the cell.

Another aspect of the present invention describes a recombinant cell produced by combining (a) a cell where a G-protein fusion receptor is expressed, and (b) a vector comprising nucleic acid encoding a G-protein fusion receptor and elements for introducing heterologous nucleic acid into the cell. Preferably, the G-protein fusion receptor is functional in the cell.

Another aspect of the present invention describes a process for the production of a G-protein fusion receptor. The process is performed by growing host cells comprising a G-protein fusion receptor.

Another aspect of the present invention describes a method of measuring the ability of a compound to affect G-protein fusion receptor activity.

Another aspect of the present invention describes a chimeric GABA_BR comprising an extracellular domain, a transmembrane domain and an intracellular domain, wherein at least one domain is from a GABA_BR and at least one domain is from CaR or mGluR8. The extracellular domain comprises an amino acid sequence substantially similar to a CaR extracellular domain (SEQ. ID. NO.

1), a GABA_AR1a extracellular domain (SEQ. ID. NO. 2), a GABA_AR1b extracellular domain (SEQ. ID. NO. 3), a GABA_AR2 extracellular domain (SEQ. ID. NO. 4), or a mGluR8 extracellular domain (SEQ. ID. NO. 5).

5 The transmembrane domain comprises an amino acid sequence substantially similar to a CaR transmembrane domain (SEQ. ID. NO. 6), a GABA_AR1a transmembrane domain (SEQ. ID. NO. 7), a GABA_AR1b transmembrane domain (SEQ. ID. NO. 8), a GABA_AR2 transmembrane domain (SEQ. ID. NO. 9), or a mGluR8 transmembrane domain (SEQ. ID. NO. 10).

10 The intracellular domain comprises an amino acid sequence substantially similar to a CaR intracellular domain (SEQ. ID. NO. 11), a GABA_AR1a intracellular domain (SEQ. ID. NO. 12), a GABA_AR1b intracellular domain (SEQ. ID. NO. 13), a GABA_AR2 intracellular domain (SEQ. ID. NO. 14), or a mGluR8 intracellular domain (SEQ. ID. NO. 15).

Preferred chimeric GABA_ARs contain at least one mGluR8 intracellular, transmembrane or extracellular domain, or at least one CaR intracellular, transmembrane or extracellular domain.
20 More preferably, the chimeric GABA_AR contains at least one CaR domain.

In preferred embodiments concerning mGluR8 regions that are present: the mGluR8 extracellular domain is substantially similar to the mGluR8 extracellular domain provided in SEQ. ID. NO. 5;
25 the mGluR8 transmembrane domain is substantially similar to the mGluR8 transmembrane domain provided in SEQ. ID. NO. 10; and the mGluR8 intracellular domain is substantially similar to the mGluR8 receptor intracellular provided in SEQ. ID. NO. 15.

Preferably, the domains are functionally coupled such that a
30 signal from the binding of an extracellular ligand is transduced to the intracellular domain when the chimeric receptor is present in a suitable host cell. A suitable host cell contains the elements for functional signal transduction for receptors coupled to a G-protein.

Another aspect of the present invention describes a nucleic acid comprising a nucleotide sequence encoding for a chimeric GABA_AR.

Another aspect of the present invention describes a
5 recombinant cell comprising an expression vector encoding for a chimeric GABA_AR, and a cell where the chimeric GABA_AR is expressed. Preferably, the chimeric GABA_AR is functional in the cell.

Another aspect of the present invention describes a
10 recombinant cell produced by combining (a) a cell where a chimeric GABA_AR is expressed, and (b) a vector comprising nucleic acid encoding the chimeric GABA_AR and elements for introducing heterologous nucleic acid into the cell. Preferably, the chimeric GABA_AR is functional in the cell.

Another aspect of the present invention describes a process
15 for the production of a chimeric receptor. The process is performed by growing host cells comprising a chimeric GABA_AR.

Another aspect of the present invention describes a method
20 of measuring the ability of a compound to affect GABA_AR or mGluR activity. The method is performed by measuring the ability of a compound to affect chimeric GABA_AR or mGluR activity.

Another aspect of the present invention describes a fusion
receptor polypeptide comprising a receptor and a G-protein α subunit, wherein said G-protein α subunit is fused to the
25 intracellular domain of said receptor, provided that the receptor is not an adrenoreceptor.

Various examples are described herein. These examples are not intended in any way to limit the claimed invention.

Other features and advantages of the invention will be
30 apparent from the following drawings, the description of the invention, the examples, and the claims.

BRIEF DESCRIPTION OF DRAWINGS

Figures 1a-1d illustrate the amino acid sequences of a human CaR extracellular domain (SEQ. ID. NO. 1), a human GABA_BR1a extracellular domain (SEQ. ID. NO. 2), a human GABA_BR1b extracellular domain (SEQ. ID. NO. 3), a human GABA_BR2 extracellular domain (SEQ. ID. NO. 4), and a human mGluR8 extracellular domain (SEQ. ID. NO. 5).

Figures 2a-2b illustrate the amino acid sequences of a human CaR transmembrane domain (SEQ. ID. NO. 6), a human GABA_BR1a transmembrane domain (SEQ. ID. NO. 7), a human GABA_BR1b transmembrane domain (SEQ. ID. NO. 8), a human GABA_BR2 transmembrane domain (SEQ. ID. NO. 9), and a human mGluR8 transmembrane domain (SEQ. ID. NO. 10).

Figures 3a-3b illustrate the amino acid sequences of a human CaR intracellular domain (SEQ. ID. NO. 11), a human GABA_BR1a intracellular domain (SEQ. ID. NO. 12), a human GABA_BR1b intracellular domain (SEQ. ID. NO. 13), a human GABA_BR2 intracellular domain (SEQ. ID. NO. 14), and a human mGluR8 intracellular domain (SEQ. ID. NO. 15).

Figures 4a-4b illustrate the amino acid sequence of G α_{i1} , (SEQ. ID. NO. 16) and G α_{i16} (SEQ. ID. NO. 17).

Figures 5a-5r illustrate the cDNA sequences encoding for human CaR (SEQ. ID. NO. 18), human GABA_BR1a (SEQ. ID. NO. 19), human GABA_BR1b (SEQ. ID. NO. 20), and human GABA_BR2 (SEQ. ID. NO. 21).

Figures 6a-6h illustrate the cDNA sequence for rat GABA_BR1a (SEQ. ID. NO. 22) and rat GABA_BR1b (SEQ. ID. NO. 23).

Figures 7a-7c illustrate the amino sequence for rat GABA_BR1a (SEQ. ID. NO. 24) and rat GABA_BR1b (SEQ. ID. NO. 25).

Figure 8 illustrates the ability of a chimeric CaR/GABA_BR2 (CaR extracellular and transmembrane domains, and intracellular GABA_BR2 domain) to transduce a signal. Signal production was measured by detecting an increase in the calcium-activated chloride current. The line in the middle of the increase signifies a wash step.

Figures 9a-9p illustrate the cDNA sequence for human mGluR2

(SEQ. ID. NO. 26), chimeric hCAR/hmGluR2 (SEQ. ID. NO. 30), chimeric hmGluR2/hCaR (SEQ. ID. NO. 34), and chimeric hmGluR8/hCaR (SEQ. ID. NO. 38).

Figures 10a-10f illustrate the amino acid sequence for human mGluR2 (SEQ. ID. NO. 27), chimeric hCAR/hmGluR2 (SEQ. ID. NO. 31), chimeric hmGluR2/hCaR (SEQ. ID. NO. 35), chimeric hmGluR8/hCaR (SEQ. ID. NO. 39).

Figures 11a-11v illustrate the cDNA sequence for the phCaR/hmGluR2*Gqi5 fusion construct (SEQ. ID. NO. 32), pmGluR2//CaR*G α i5 fusion construct (SEQ. ID. NO. 36), pmGluR2//CaR*G α i5+3Ala linker fusion construct (SEQ. ID. NO. 46), and the mGluR8//CaR*G α i5 fusion construct (SEQ. ID. NO. 40).

Figures 12a-12h illustrate the amino acid sequence for the phCaR/hmGluR2*Gqi5 fusion construct (SEQ. ID. NO. 33), pmGluR2//CaR*G α i5 fusion construct (SEQ. ID. NO. 37), pmGluR2//CaR*G α i5+3Ala linker fusion construct (SEQ. ID. NO. 47), and the mGluR8//CaR*G α i5 fusion construct (SEQ. ID. NO. 41).

Figures 13a-13m illustrate the cDNA sequence for the GABA-R2*Gqo5 fusion construct (SEQ. ID. NO. 42) and the GABA-BR1a*Gqo5 fusion construct (SEQ. ID. NO. 44).

Figures 14a-14e illustrates the amino acid sequence for the GABA-BR2*Gqo5 fusion construct (SEQ. ID. NO. 43) and the GABA-BR1a*Gqo5 fusion construct (SEQ. ID. NO. 45).

Figure 15 illustrates the ability of different G-protein fusions to transduce signal resulting from ligand binding. mGluR2//CaR*Gqi5 is shown by SEQ. ID. NO. 37, CaR/mGluR2*Gqi5 is shown by SEQ. ID. NO. 33, mGluR8//CaR*Gqi5 is shown by SEQ. ID. NO. 41.

DETAILED DESCRIPTION OF THE INVENTION

The CaR, mGluR, and the GABA_AR are structurally similar in that they are each a single subunit membrane protein possessing an extracellular domain, a transmembrane domain comprising seven putative membrane spanning helices connected by three intracellular and three extracellular loops, and an intracellular

carboxy-terminal domain. Signal transduction is activated by the extracellular binding of an agonist. The signal is transduced to the intracellular components of the receptor causing an intracellular effect.

5 Signal transduction from agonist binding to an extracellular region can be modulated by compounds acting at a downstream transmembrane domain or the intracellular domain. Downstream effects include antagonist actions of compounds and allosteric actions of compounds.

10 The transmembrane domain provides different types of target sites for compounds modulating receptor activity in different environments. As noted above, the transmembrane domain contains extracellular, transmembrane, and intracellular components.

15 Compounds modulating GABA_AR, CaR, or mGluR activity can be obtained, for example, by screening a group or library of compounds to identify those compounds having the desired activity and then synthesizing such compound. Thus, included in the present invention is a method of making a GABA_AR, CaR, or mGluR active compound by first screening for a compound having desired
20 properties and then chemically synthesizing that compound.

Metabotropic Glutamate Receptors (mGluRs)

mGluRs are G protein-coupled receptors capable of activating a variety of intracellular secondary messenger systems following
25 the binding of glutamate (Schoepp et al., *Trends Pharmacol. Sci.* 11:508, 1990; Schoepp and Conn, *Trends Pharmacol. Sci.* 14:13, 1993, hereby incorporated by reference herein).

Activation of different mGluR subtypes in situ elicits one or more of the following responses: activation of phospholipase C,
30 increases in phosphoinositide (PI) hydrolysis, intracellular calcium release, activation of phospholipase D, activation or inhibition of adenylyl cyclase, increases and decreases in the formation of cyclic adenosine monophosphate (cAMP), activation of guanylyl cyclase, increases in the formation of cyclic guanosine
35 monophosphate (cGMP), activation of phospholipase A₂, increases in

arachidonic acid release, and increases or decreases in the activity of voltage- and ligand-gated ion channels (Schoepp and Conn, *Trends Pharmacol. Sci.* 14:13, 1993; Schoepp, *Neurochem. Int.* 24:439, 1994; Pin and Duvoisin, *Neuropharmacology* 34:1, 1995, hereby incorporated by reference herein).

5 Eight distinct mGluR subtypes have been isolated. (Nakanishi, *Neuron* 13:1031, 1994; Pin and Duvoisin, *Neuropharmacology* 34:1, 1995; Knopfel et al., *J. Med. Chem.* 38:1417; *Eur. J. Neuroscience* 7:622-629, 1995, each of these references is hereby incorporated
10 by reference herein.) The different mGluRs possess a large amino-terminal extracellular domain (ECD) followed by seven putative transmembrane domain (7TMD) comprising seven putative membrane spanning helices connected by three intracellular and three
15 extracellular loops, and an intracellular carboxy-terminal domain of variable length (cytoplasmic tail).

Human mGluR8 is described by Stormann et al., International Application Number PCT/US97/09025, International Publication Number WO 97/48724, and mouse mGluR8 is described by Duvoisin et al., *J. Neurosci.* 15:3075-3083, 1995, (both of these references
20 are hereby incorporated by reference herein). mGluR8 couples to G_i . Agonists of mGluR8 include L-glutamate and L-2-amino-4-phosphonobutyrate.

mGluR8 activity can be measured using standard techniques. For example, G_i negatively couples to adenylate cyclase to inhibit
25 intracellular cAMP accumulation in a pertussis toxin-sensitive fashion. Thus, mGluR8 activity can be measured, for example, by measuring inhibition of forskolin-stimulated cAMP production as described by Duvoisin et al., *J. Neurosci.* 15:3075-3083, 1995.

mGluRs have been implicated in a variety of neurological
30 pathologies. Examples of such pathologies include stroke, head trauma, spinal cord injury, epilepsy, ischemia, hypoglycemia, anoxia, and neurodegenerative diseases such as Alzheimer's disease (Schoepp and Conn, *Trends Pharmacol. Sci.* 14:13, 1993; Cunningham et al., *Life Sci.* 54: 135, 1994; Pin et al.,
35 *Neuropharmacology* 34:1, 1995; Knopfel et al., *J. Med. Chem.*

38:1417, 1995, each of which is hereby incorporated by reference herein).

Calcium Receptor

5 The CaR responds to changes of extracellular calcium concentration and also responds to other divalent and trivalent cations. The CaR is a G-protein coupled receptor containing an extracellular Ca^{2+} binding domain. Activation of the CaR, descriptions of CaRs isolated from different sources, and
10 examples of CaR active compound are provided in Nemeth NIPS 10:1-5, 1995, Brown et al. U.S. Patent No. 5,688,938, Van Wagenen et al., International Application Number PCT/US97/05558 International Publication Number WO 97/37967, Brown E.M. et al., Nature 366:575, 1993, Riccardi D., et al., Proc. Nat'l. Acad.
15 Sci. USA 92:131-135, 1995, and Garrett J.E., et al., J. Biol. Chem. 31:12919-12925, 1995. (Each of these references are hereby incorporated by reference herein.) Brown et al. U.S. Patent No. 5,688,938 and Van Wagenen et al., International Application
20 Number PCT/US97/05558 International Publication Number WO 97/37967, describe different types of compounds active at the CaR including compounds which appear to be allosteric modulators and CaR antagonists.

 The CaR can be targeted to achieve therapeutic effects. Examples of target diseases are provided in Brown et al. U.S.
25 Patent No. 5,688,938, and Van Wagenen et al., International Application Number PCT/US97/05558 International Publication Number WO 97/37967, and include hyperparathyroidism and osteoporosis.

γ -Aminobutyric acid Receptors (GABA_A Rs)

30 GABA_A Rs are G-protein coupled metabotropic receptors. GABA_A Rs modulate synaptic transmission by inhibiting presynaptic transmitter release and by increasing K^+ conductance responsible for long-lasting inhibitory postsynaptic potentials. (See,

Kaupmann et al., *Nature* 386:239-246, 1997, hereby incorporated by reference herein.)

GABA_ARs are found in the mammalian brain, in locations outside of the brain, and in lower species. Outside of the brain, GABA_ARs have been identified on axon terminals and ganglion cell bodies of the autonomic nervous system, on fallopian tube and uterine intestinal smooth muscle cells, in the kidney cortex, urinary bladder muscle and on testicular interstitial cells. (See, Bowery, *Annu. Rev. Pharmacol. Toxicol.* 33:109-147, 1993, hereby incorporated by reference herein.)

Different GABA_ARs subtypes exist. Kaupmann et al., *Nature* 386:239-246, 1997, indicate that they cloned GABA_ARs. Nucleic acid encoding two GABA_AR proteins were indicated to be cloned from rat brain: GABA_AR1a and GABA_AR1b. GABA_AR1a differs from GABA_AR1b in that the N-terminal 147 residues are replaced by 18 amino acids. GABA_AR1a and GABA_AR1b appear to be splice variants. The cloned GABA_ARs were indicated to negatively couple adenylyl cyclases and show sequence similarity to the metabotropic receptors for L-glutamate (mGluR). Northern blot analysis indicated that GABA_AR1a and GABA_AR1b is present in brain and testis, but not in kidney, skeletal muscle, liver, lung, spleen, or heart.

Kaupmann et al., International Application Number PCT/EP97/01370, International Publication Number WO 97/46675, indicate that they have obtained rat GABA_AR clones, GABA_AR1a and GABA_AR1b; and humans GABA_AR clones, GABA_AR1a/b (representing a partial receptor clone) and GABA_AR1b (representing a full-length receptor clone). Amino acid sequence information, and encoding cDNA sequence information, is provided for the different GABA_AR clones.

Another GABA_AR subtype is GABA_AR2. Northern blot analysis reveals that an approximately 6.3 Kb human GABA_AR2 transcript is abundantly expressed in the human brain. Expression is not detected in the heart, placenta, lung, liver, skeletal muscle, kidney and pancreas under conditions where GABA_AR2 transcript was

identified in the human brain. Within the human brain GABA_AR2 is broadly expressed at variable levels.

GABA_AR functions as a heterodimer of the subunits GABA_AR1 or GABA_AR2. (Jones et al. *Nature* 396:674-679, 1998, hereby
5 incorporated by reference herein.)

GABA_ARs have been targeted to achieve therapeutic effects. Kerr and Ong, *DDT* 1:371-380, 1996, describe different compounds indicated to be GABA_AR agonists and GABA_AR antagonists. Kerr and Ong also review therapeutic implications of affecting GABA_AR
10 activity including, spasticity and motor control, analgesia, epilepsy, cognitive effects, psychiatric disorders, alcohol dependence and withdrawal, feeding behavior, cardiovascular and respiratory functions, and peripheral functions.

Bittiger et al., *Tips* 4:391-394, 1993, review therapeutic
15 applications of GABA_AR antagonists. Potential therapeutic applications noted by Bittiger et al. include cognitive processes, epilepsy, and depression.

G-Protein Fusion Receptors

20 Examples of some different types of G-protein fusion receptors, and advantages of some receptors, are provided below. Using the present application as guide additional G-protein receptors fusion can be constructed.

G-protein fusion receptors contain an intracellular domain
25 of a receptor fused to a G-protein α subunit (G_α). G_α fusions to adrenoceptors have been reported by Bertin et al., *Receptors and Channels* 5:41-51, 1997; Wise and Milligan, *Journal of Biological Chemistry* 39:24673-24678, 1997; and Bertin et al., *Proc. Natl. Acad. Sci. USA* 91:8827-8831, 1994 (each of which are
30 hereby incorporated by reference herein). These studies were indicated to produce a functional chimeric by fusing the α_{2A} -adrenoceptor to the $G_{11\alpha}$, or the β_2 -adrenoceptor to the $G_{s\alpha}$.

The G-protein fusion receptors described by the present invention include a G-protein fused to an intracellular domain,
35 where the intracellular domain when present in a wild type

receptor does not interact with that type of G-protein. Thus, the present invention also describes swapping of signals by fusing an intracellular domain to a G_α normally not coupled to that intracellular domain. The use of such fusion proteins, while applicable to chimeric GABA_ARs, is not limited to chimeric GABA_ARs. Indeed, such technology can be applied to receptors containing an extracellular domain, transmembrane domain and intracellular domain of a wild type receptor.

Preferred G-proteins fusion receptors contain an intracellular domain fused to a promiscuous G_α that couples to phospholipase C resulting in the mobilization of intracellular calcium. Increases in intracellular calcium can be conveniently measured through the use of dyes. Such techniques are well known in the art and are described, for example by Brown et al. U.S. Patent No. 5,688,938.

In an embodiment G-proteins fusions can also be used to decrease receptor desensitization.

Examples of promiscuous G_α 's coupling to phospholipase C include naturally occurring G-proteins such as $G_{\alpha 15}$ and $G_{\alpha 16}$, and chimeric G-protein such as Gqo5 and Gqi5. Gqo5 and Gqi5 are made of a Gq portion where the five amino acids at the C-terminal are from either G_o or G_i , respectively (Conklin et al., *Nature* 363:274-277, 1993, hereby incorporated by reference herein). The Gq portion of such chimeric receptors provides for phospholipase C coupling while the terminal G_o or G_i portion allows the chimeric G-protein to couple to different receptor proteins that are normally involved in inhibitor effects on adenylate cyclase.

In an embodiment of the present invention the employed G-protein is from a human source or is made up of different G-protein components each from a human source.

G-proteins fusions can be created, for example, by fusing directly or indirectly the intracellular domain of a receptor protein to a polypeptide having an amino acid sequence substantially similar to $G_{\alpha 15}$, $G_{\alpha 16}$, Gqo5 or Gqi5. In different embodiments, the receptor is fused directly or indirectly to a G-

protein consisting of the amino acid sequence of $G_{\alpha 15}$, $G_{\alpha 16}$, G_{qo5} or G_{qi5} .

The intracellular domain portion of a receptor protein fused directly or indirectly to a G-protein should be at least about 10 amino acids in length. In different embodiments the portion is at least about 50 amino acids, at least about 100 amino acids, or the full length of an intracellular domain.

The intracellular domain can be directly linked to a G-protein or can be indirectly linked through an optionally present linker. Optionally present linkers are preferably about 3 to about 30 amino acids in length. Preferred linkers are made up of alanine, glycine, or a combination thereof.

Chimeric Receptors

Examples of some different types of chimeric receptors, and advantages of some receptors, are provided below. Using the present application as guide additional chimeric receptors can be constructed.

20 Chimeric GABA_AR Extracellular Domain

Chimeric GABA_ARs containing a GABA_AR extracellular domain are particularly useful for studying the importance of the GABA_AR extracellular domain and assaying for compounds active at the extracellular domain. Preferably chimeric GABA_ARs containing a GABA_AR extracellular domain also contain a CaR intracellular domain.

A variety of different activities have been generally attributed to GABA_AR subtypes. (E.g., Kerr and Ong, DDT 1:371-380, 1996.) Kaupmann et al., Nature 386:239-246, 1997, report that in preliminary experiments involving GABA_AR1a they did not detect positive coupling to the adenylyl cyclase or coupling to the phospholipase effector system.

An intracellular CaR domain can be used to couple with G-proteins which activate phospholipase C and mobilize intracellular calcium. Mobilization of intracellular calcium is

readily detected, for example, by fluorescent indicators of intracellular Ca^{2+} .

An additional advantage of using the intracellular CaR domain is that CaR G-protein activation is not rapidly desensitized. Thus, the intracellular CaR domain can be used to produce a stronger intracellular signal than a signal produced from a receptor which is desensitized rapidly.

More preferably, the chimeric GABA_BR contains an intracellular CaR domain, and also contains either a CaR or a GABA_BR transmembrane domain. Advantages of using a CaR transmembrane domain include separating the effects occurring at a GABA_BR extracellular domain from effects occurring at a transmembrane domain; and providing additional intracellular elements, present on transmembrane intracellular loops, useful for coupling to G-protein.

A GABA_BR transmembrane domain is useful for examining whether the transmembrane GABA_BR can be targeted to affect GABA_BR activity, and obtaining compounds active at the GABA_BR transmembrane domain. For example, a transmembrane GABA_BR can be used to screen for transmembrane allosteric modulators and antagonists.

Chimeric GABA_BR Transmembrane Domain

Chimeric GABA_BRs containing a GABA_BR transmembrane are particularly useful for studying the importance of the GABA_BR transmembrane domain and assaying for compounds active at the transmembrane domain. Preferably Chimeric GABA_BRs containing a GABA_BR transmembrane domain contain an extracellular domain which is either mGluR8 or CaR, and an intracellular CaR domain.

More preferably, the chimeric GABA_BR contains an extracellular domain from either mGluR8 or CaR, a GABA_BR transmembrane, and an intracellular CaR domain. A chimeric GABA_BR containing extracellular mGluR8 or CaR domains can readily be stimulated using mGluR8 or CaR ligands.

Chimeric GABA_AR Intracellular Domain

Chimeric GABA_ARs containing a GABA_AR intracellular domain are particularly useful for studying the importance of the GABA_AR intracellular domain and assaying for compounds active at the intracellular domain. Preferably, the chimeric receptors contain an extracellular domain from either mGluR8 or CaR. The extracellular mGluR8 or CaR domains can readily be activated using mGluR8 or CaR ligands.

Receptor Domains

Domains of a G-protein fusion receptor, a chimeric receptor, and G_q, substantially similar to a particular sequence can be readily produced using the disclosure provided herein in conjunction with information well known in the art. Substantially similar sequences can be obtained taking into account sequence information for a particular type of receptor obtained from different sources, different types of amino acids which are to some extent interchangeable, and the ease of experimentation with which functional receptor activity can be assayed.

Substantially similar sequences includes amino acid alterations such as deletions, substitutions, additions, and amino acid modifications. A "deletion" refers to the absence of one or more amino acid residue(s) in the related polypeptide. An "addition" refers to the presence of one or more amino acid residue(s) in the related polypeptide. Additions and deletions to a polypeptide may be at the amino terminus, the carboxy terminus, and/or internal. Amino acid "modification" refers to the alteration of a naturally occurring amino acid to produce a non-naturally occurring amino acid. A "substitution" refers to the replacement of one or more amino acid residue(s) by another amino acid residue(s) in the polypeptide. Derivatives can contain different combinations of alterations including more than one alteration and different types of alterations.

The sequences of polypeptides can be compared from different sources to help identify variable amino acids not essential for receptor activity. For example, Figure 7 provides the rat GABA_AR1a and GABA_AR1b amino acid sequences. The rat GABA_AR1a and GABA_AR1b amino acid sequences can be compared with the human GABA_AR1a and GABA_AR1b sequences to identify conserved and variable amino acids. Derivatives can then be produced where a variable amino acid is changed, and receptor activity can be readily tested.

10 Similarly, the amino acid sequences for CaR, mGluR8, and G-proteins from different sources are either known in the art or can readily be obtained. Examples of such references are provided above.

15 While the effect of an amino acid change varies depending upon factors such as phosphorylation, glycosylation, intra-chain linkages, tertiary structure, and the role of the amino acid in the active site or a possible allosteric site, it is generally preferred that a substituted amino acid is from the same group as the amino acid being replaced. To some extent the following groups contain amino acids which are interchangeable: the basic amino acids lysine, arginine, and histidine; the acidic amino acids aspartic and glutamic acids; the neutral polar amino acids serine, threonine, cysteine, glutamine, asparagine and, to a lesser extent, methionine; the nonpolar aliphatic amino acids 25 glycine, alanine, valine, isoleucine, and leucine (however, because of size, glycine and alanine are more closely related and valine, isoleucine and leucine are more closely related); and the aromatic amino acids phenylalanine, tryptophan, and tyrosine. In addition, although classified in different categories, alanine, 30 glycine, and serine seem to be interchangeable to some extent, and cysteine additionally fits into this group, or may be classified with the polar neutral amino acids.

While proline is a nonpolar neutral amino acid, its replacement represents difficulties because of its effects on 35 conformation. Thus, substitutions by or for proline are not

preferred, except when the same or similar conformational results can be obtained. The conformation conferring properties of proline residues may be obtained if one or more of these is substituted by hydroxyproline (Hyp).

5 Examples of modified amino acids include the following:

altered neutral nonpolar amino acids such as ω -amino acids of the formula $H_2N(CH_2)_nCOOH$ where n is 2-6, sarcosine (Sar), t-butylalanine (t-BuAla), t-butylglycine (t-BuGly), N-methyl isoleucine (N-MeIle), and norleucine (Nleu); altered neutral
10 aromatic amino acids such as phenylglycine; altered polar, but neutral amino acids such as citrulline (Cit) and methionine sulfoxide (MSO); altered neutral and nonpolar amino acids such as cyclohexyl alanine (Cha); altered acidic amino acids such as cysteic acid (Cya); and altered basic amino acids such as
15 ornithine (Orn).

Preferred derivatives have one or more amino acid alteration(s) which do not significantly affect the receptor activity of the related receptor protein. In regions of receptor domains not necessary for receptor activity, amino acids may be
20 deleted, added or substituted with less risk of affecting activity. In regions required for receptor activity, amino acid alterations are less preferred as there is a greater risk of affecting receptor activity.

Derivatives can be produced using standard chemical
25 techniques and recombinant nucleic acid techniques.

Modifications to a specific polypeptide may be deliberate, as through site-directed mutagenesis and amino acid substitution during solid-phase synthesis, or may be accidental such as through mutations in hosts which produce the polypeptide.

30 Polypeptides including derivatives can be obtained using standard techniques such as those described by Sambrook et al., *Molecular Cloning*, Cold Spring Harbor Laboratory Press (1989). For example, Chapter 15 of Sambrook describes procedures for site-directed mutagenesis of cloned DNA.

Receptor Nucleic Acid

G-protein fusion and chimeric receptor nucleic acid can be produced based on the information provided herein along with standard recombinant nucleic acid techniques. Examples of references describing recombinant nucleic acid techniques include
5 *Molecular Cloning*, Sambrook et al., Cold Spring Harbor Laboratory Press (1989); and *Current Protocols in Molecular Biology*, Frederick et al., John Wiley & Sons, Inc. (1995).

Due to the degeneracy of the genetic code different nucleic acid sequences can encode for a particular polypeptide. Thus, a
10 large number of nucleic acids encoding for a receptor having the same amino acid sequence can be produced.

An embodiment of the present invention uses human nucleic acid encoding for the domains from CaR, GABA_AR1A, GABA_AR1B,
15 GABA_AR2 and/or mGluR8. The amino acid sequences of different domains is provided in Figures 1-3.

Recombinant Cells

Nucleic acid expressing a functional G-Protein fusion or a
20 chimeric receptor can be used to create transfected cells lines expressing such receptors. Such cell lines have a variety of uses such as being used for high-throughput screening for compounds modulating receptor activity; being used to assay binding to the receptor; and as factories to produce large
25 amounts of a receptor.

A variety of cell lines can couple exogenously expressed receptors to endogenous functional responses. Cell lines such as NIH-3T3, HeLa, NG115, CHO, HEK 293 and COS7 which are expected to lack CaR, mGluR8, and GABA_AR can be tested to confirm that they
30 lack these receptors.

Production of stable transfectants can be accomplished by transfection of an appropriate cell line with, for example, an expression vector such as pMSG vector, in which the coding sequence for the G-protein fusion or chimeric GABA_AR cDNA has been
35 cloned. Expression vectors containing a promoter region, such as

the mouse mammary tumor virus promoter (MMTV), drive high-level transcription of cDNAs in a variety of mammalian cells. In addition, these vectors contain genes for selecting cells stably expressing cDNA of interest. The selectable marker in the pMSG
5 vectors encode an enzyme, xanthine-guanine phosphoribosyl transferase (XGPRT), conferring resistance to a metabolic inhibitor that is added to the culture to kill nontransfected cells.

The most effective method for transfection of eukaryotic
10 cell lines with plasmid DNA varies with the given cell type. The expression construct will be introduced into cultured cells by the appropriate technique, such as Ca^{2+} phosphate precipitation, DEAE-dextran transfection, lipofection or electroporation.

Expression of the receptor cDNA in cell lines can be
15 assessed by solution hybridization and Northern blot analysis.

Binding Assays

The present invention also includes using G-protein fusion receptors or chimeric GABA_BR in a binding assay. G-protein fusion
20 receptors or chimeric GABA_BRs having a particular GABA_BR domain can be used, for example to facilitate obtaining compounds able to bind to that particular receptor domain; and to determine whether a compound which binds to a particular domain. For example, in a complete chimeric GABA_BR containing extracellular,
25 transmembrane, and intracellular domains, the presence of one or more domains from CaR or mGluR are useful to present GABA_BR domain(s) to a binding agent in a form more like the GABA_BR domain(s) in the wild type receptor compared to an incomplete GABA_BR receptor fragment lacking one or more domains.

30 Binding assays can be carried out using techniques well known in the art. Binding assays preferably employ radiolabeled binding agents.

An example of a binding procedure is carried out by first attaching chimeric GABA_BR to a solid-phase support to create an
35 affinity matrix. The affinity matrix is then contacted with

potential GABA_AR binding agents. A large library of compounds may be used to determine those compounds binding to the affinity matrix. Bound compounds can be eluted from the column.

5

Therapeutic Modulation

As pointed out above, different types of diseases and disorders can be treated using compounds modulating CaR, mGluR, or GABA_AR activity. Additionally, such compounds can be used prophylactically. Compounds modulating GABA_AR2 activity can be administered to patients who would benefit from such treatment. Patients are mammals, preferably humans.

Modulators of CaR, mGluR, or GABA_AR activity can be administered to a patient using standard techniques. Techniques and formulations generally may be found in Remington's
15 Pharmaceutical Sciences, 18th ed., Mack Publishing Co., Easton, PA, 1990 (hereby incorporated by reference herein).

Suitable dosage forms, in part, depend upon the use or the route of entry, for example, oral, transdermal, transmucosal, or by injection (parenteral). Such dosage forms should allow the therapeutic agent to reach a target cell whether the target cell is present in a multicellular host or in culture. For example, pharmacological compounds or compositions injected into the blood stream should be soluble. Other factors are well known in the art, and include considerations such as toxicity and dosage forms which retard the therapeutic agent from exerting its effect.

Therapeutic compounds can be formulated as pharmaceutically acceptable salts and complexes thereof. Pharmaceutically acceptable salts are non-toxic salts in the amounts and concentrations at which they are administered. The preparation of such salts can facilitate the pharmacological use by altering the physical characteristics of the compound without preventing it from exerting its physiological effect. Useful alterations in physical properties include lowering the melting point to facilitate transmucosal administration and increasing the

solubility to facilitate administering higher concentrations of the drug.

The pharmaceutically acceptable salt of a compound may be present as a complex. Examples of complexes include an 8-chlorotheophylline complex (analogous to, e.g.,
5 dimenhydrinate:diphenhydramine 8-chlorotheophylline (1:1) complex; Dramamine) and various cyclodextrin inclusion complexes.

Pharmaceutically acceptable salts include acid addition salts such as those containing sulfate, hydrochloride, fumarate,
10 maleate, phosphate, sulfamate, acetate, citrate, lactate, tartrate, methanesulfonate, ethanesulfonate, benzenesulfonate, p-toluenesulfonate, cyclohexylsulfamate and quinate.

Pharmaceutically acceptable salts can be obtained from acids such as hydrochloric acid, maleic acid, sulfuric acid, phosphoric
15 acid, sulfamic acid, acetic acid, citric acid, lactic acid, tartaric acid, malonic acid, methanesulfonic acid, ethanesulfonic acid, benzenesulfonic acid, p-toluenesulfonic acid, cyclohexylsulfamic acid, fumaric acid, and quinic acid.

Pharmaceutically acceptable salts also include basic
20 addition salts such as those containing benzathine, chloroprocaine, choline, diethanolamine, ethylenediamine, meglumine, procaine, aluminum, calcium, lithium, magnesium, potassium, sodium, ammonium, alkylamine, and zinc, when acidic functional groups, such as carboxylic acid or phenol are present.
25 For example, see Remington's Pharmaceutical Sciences, 18th ed., Mack Publishing Co., Easton, PA, p. 1445, 1990. Such salts can be prepared using the appropriate corresponding bases.

Carriers or excipients can also be used to facilitate administration of therapeutic agents. Examples of carriers
30 include calcium carbonate, calcium phosphate, various sugars such as lactose, glucose, or sucrose, or types of starch, cellulose derivatives, gelatin, vegetable oils, polyethylene glycols and physiologically compatible solvents. Examples of physiologically compatible solvents include sterile solutions of water for
35 injection (WFI), saline solution and dextrose.

GABA_BR modulating compounds can be administered by different routes including intravenous, intraperitoneal, subcutaneous, intramuscular, oral, topical (transdermal), or transmucosal administration. For systemic administration, oral administration
5 is preferred. For oral administration, for example, the compounds can be formulated into conventional oral dosage forms such as capsules, tablets, and liquid preparations such as syrups, elixirs, and concentrated drops.

Alternatively, injection (parenteral administration) may be
10 used, e.g., intramuscular, intravenous, intraperitoneal, and subcutaneous. For injection, compounds are formulated in liquid solutions, preferably, in physiologically compatible buffers or solutions, such as saline solution, Hank's solution, or Ringer's solution. In addition, the compounds may be formulated in solid
15 form and redissolved or suspended immediately prior to use. Lyophilized forms can also be produced.

Systemic administration can be by transmucosal or transdermal means. For transmucosal or transdermal administration, penetrants appropriate to the barrier to be
20 permeated are used in the formulation. Such penetrants are well known in the art, and include, for example, for transmucosal administration, bile salts and fusidic acid derivatives. In addition, detergents may be used to facilitate permeation. Transmucosal administration, for example, may be through nasal
25 sprays, rectal suppositories, or vaginal suppositories.

For topical administration, compounds can be formulated into ointments, salves, gels, or creams, as is well known in the art.

The amounts of various GABA_BR modulating compounds to be administered can be determined by standard procedures taking into
30 account factors such as the compound IC₅₀, EC₅₀, the biological half-life of the compound, the age, size and weight of the patient, and the disease or disorder associated with the patient. The importance of these and other factors to be considered are well known to those of ordinary skill in the art. Generally, the

amount is expected to preferably be between about 0.01 and 50 mg/kg of the animal to be treated.

EXAMPLES

5 Examples are provided below illustrating different aspects and embodiments of the present invention. The examples include techniques that can be used to produce and use G-protein fusion receptors and chimeric receptors. These examples are not intended to limit the claimed invention.

10

Example 1: Construction of G-Protein Fusions

 This example illustrates different G-protein fusion receptor constructs and techniques used to produce different G-protein fusion receptor constructs. Numbering of nucleotide position for
15 all the following constructs is such that nucleotide number 1 corresponds to the A of the ATG start codon of the nucleotide sequence encoding the designated protein.

I. FULL-LENGTH CONSTRUCTS

20 A. phCaR

 The cDNA encoding the human CaR (Garrett et al., (1995) J. Biol. Chem. 270:12919) is harbored in the Bluescript SK(-) plasmid (Stratagene). This construct is referred to as phCaR.

25 B. phmGluR2

 A full length human mGluR2 cDNA was amplified from human cerebellum MarathonReady cDNA (Clontech) using PCR primers based on the human mGluR2 cDNA sequence (Genbank Accession # 4504136). The obtained PCR fragment was subcloned into the pT7Blue TA
30 vector (Novagen). A Hind III-Not I fragment containing the human mGluR2 cDNA was then subcloned into the Bluescript SKII(-) plasmid (Stratagene). This construct is referred to as phmGluR2.

C. phGα_q

35 A full length human Gα_q cDNA was amplified from human cerebral cortex Quick-Clone cDNA (Clontech) using PCR primers based on the human Gα_q cDNA sequence (Genbank Accession # 4504044). The obtained PCR fragment was subcloned into the

Bluescript SKII(-) plasmid (Stratagene). This construct is referred to as phG α _Q.

D. phmGluR8

5 The cDNA encoding the full length human mGluR8 cDNA (Stormann et al., International Publication No. WO97/48724) is harbored in the Bluescript SKII(-) plasmid (Stratagene). This construct is referred to as phmGluR8.

10 II. G α q15

 The cDNA encoding the human G α q15 cDNA (Conklin et al (1993) Nature 363:274-77) is harbored in the Bluescript SKII(-) plasmid (Stratagene). This construct is referred to as G α q15. The nucleic acid and amino acid sequences for G α q15 are provided by
15 SEQ. ID. NOS. 28 and 29 respectively.

III. phCaR/hmGluR2

 This chimera contains the extracellular domain of the human CaR and transmembrane domain and intracellular cytoplasmic tail
20 of human mGluR2. The chimeric junction between the CaR and hmGluR2 was created using a recombinant PCR strategy similar to those described above.

 The first reaction used two primers, CA1156 (sense 19-mer, corresponding to nucleotides 1156-1174 of human CaR), and the
25 hybrid primer CA/2 (antisense 42-mer, containing 21 nucleotides complementary to nucleotides 1774-1794 of human CaR and 21 nucleotides complementary to nucleotides 1660-1680 of the human mGluR2). These primers were used to amplify a 659 bp PCR fragment of human CaR.

30 In a separate PCR reaction using phmGluR2 as template, a 692 bp fragment of the human mGluR2 was amplified using a hybrid primer 2/CA (sense 42-mer, exactly complementary to primer CA/2) and oligo 2-2330m, (antisense 23-mer, complementary to nucleotides 2309-2331 of the human mGluR2 cDNA). The two PCR
35 products generated from the above two reactions were annealed together in equimolar ratios in the presence of the external primers CA1156 and 2-2330m, and the Pfu DNA polymerase (Stratagene).

The resulting chimeric PCR product was digested with SexA1 (Boehringer Mannheim) and BamHI (New England Biolabs) and subcloned into phCaR digested with the same two restriction enzymes. In the final cloning step, the 3' end of human mGluR2 was subcloned into this construct using the restriction enzymes BsrGI and BamHI (both New England Biolabs). The sequence of the resultant chimeric construct, phCaR/hmGluR2, was verified by ABI automated DNA sequence analysis.

10 IV. phCaR/hmGluR2*Gqi5

This construct contains the phCaR/hmGluR2 chimeric receptor fused to human G α _{qi5}. A HindIII-BamHI fragment containing the phCaR/hmGluR2 construct was subcloned into pcDNA3.1/Hygro(+) (Invitrogen) to aid in constructing this fusion protein. The chimeric junction between the C-terminus of phCaR/hmGluR2 and the N-terminus of G α _{qi5} was created using a recombinant PCR strategy similar to those described above.

The first reaction used two primers, 2-1713 (sense 21-mer, corresponding to nucleotides 1710-1730 of human mGluR2) and the hybrid primer 2/Q (antisense 42-mer, containing 21 nucleotides complementary to nucleotides 2596-2616 of human mGluR2, and 21 nucleotides complementary to nucleotides 1-21 of pG α _{qi5}). These primers were used to amplify a 927 bp PCR fragment of phCaR/hmGluR2. In a separate PCR reaction all of G α _{qi5} was amplified using a hybrid primer Q/2 (sense 42-mer, exactly complementary to primer 2/Q) and the and the T3 primer commercially available from Stratagene.

These two PCR products generated from the above two reactions were annealed together in equimolar ratios in the presence of the external primers 2-1713 and T3, and the Pfu DNA polymerase (Stratagene). The resulting chimeric PCR product was digested with Bsu361 and BamHI (New England Biolabs) and subcloned into phCaR/hmGluR2 digested with the same two restriction enzymes. The sequence of the resultant chimeric fusion construct, phCaR/hmGluR2*G α _{qi5}, was verified by DNA sequence analysis.

V. phmGluR2//CaR Construct

This chimera contains the extracellular and transmembrane domains of human mGluR2 linked to the intracellular cytoplasmic tail domain of the human CaR. The chimeric junction was created
5 using three separate PCR reactions.

The first reaction used two primers, 2-1713 (sense 21-mer, corresponding to nucleotides 1710-1730 of human mGluR2, Genbank Accession # 4504136) and the hybrid primer 2/CT (antisense 42-mer, containing 21 nucleotides complementary to nucleotides 2452
10 - 2472 of human mGluR2 and 21 nucleotides complementary to nucleotides 2602-2622 of the human CaR). These primers were used to amplify a 783 bp PCR fragment of human mGluR2. In a separate PCR reaction using phCaR in the BlueScript SK⁻ plasmid as
15 template, a 750 bp fragment of the human CaR was amplified using a hybrid primer CT/2 (sense 42-mer, exactly complementary to primer 2/CT) and the T3 primer commercially available from Stratagene.

The two PCR products generated from the above two reactions were annealed together in equimolar ratios in the presence of the
20 external primers 2-1713 and T3, and the Pfu DNA polymerase (Stratagene). The resulting chimeric PCR product was digested with BsrG I and Not I (New England Biolabs) and subcloned into pmGluR2 digested with the same two restriction enzymes. The sequence of the resultant chimeric construct, pmGluR2//CaR, was
25 verified by ABI automated DNA sequence analysis.

VI. pmGluR2//CaR*Gα_qi5 Construct

This construct contains the hmGluR2//CaR chimeric receptor fused to human Gα_qi5. The chimeric junction between the C-
30 terminus of hmGluR2//CaR and the N-terminus of Gα_qi5 was created using a recombinant PCR strategy similar to that described above for the construction of phmGluR2//CaR.

The first reaction used two primers, CRP10A (sense 18-mer, corresponding to nucleotides 2812-2829 of phCaR) and the hybrid
35 primer CaRQ (antisense 42-mer, containing 21 nucleotides complementary to nucleotides 3214- 3234 phCaR, and 21 nucleotides complementary to nucleotides 1-21 of pGα_qi5). These primers were used to amplify a 443 bp PCR fragment of hmGluR2//CaR. In a

separate PCR reaction, all of $G\alpha_{q15}$ was amplified using a hybrid primer QCaR (sense 42-mer, exactly complementary to primer CaRQ) and the T3 primer commercially available from Stratagene.

The two PCR products generated from the above two reactions were annealed together in equimolar ratios in the presence of the external primers CRP10A and T3, and the Pfu DNA polymerase (Stratagene). The resulting chimeric PCR product was digested with BstE II and Not I (New England Biolabs) and subcloned into pmGluR2//CaR digested with the same two restriction enzymes. The sequence of the resultant chimeric fusion construct, pmGluR2//CaR* $G\alpha_{q15}$, was verified by ABI automated DNA sequence analysis.

VII. Fusion Receptor Protein Linker Addition Constructs

A. phmGluR2//CaR*AAA* $G\alpha_{q15}$

A linker encoding three alanine residues was incorporated into the phmGluR2//CaR* $G\alpha_{q15}$ construct by mutagenesis (Stratagene QuickChange Mutagenesis Kit). A sense 40-mer, 2CQ+LP, contained 16 nucleotides corresponding to 3219-3234 of human CaR, followed by the 9 nucleotide sequence (GCGGCCGCC) encoding three alanine residues and a NotI restriction enzyme site, and then 15 nucleotides corresponding to nucleotides 1-15 of $G\alpha_{q15}$. 2CQ+LP was annealed to an antisense 40-mer, 2CQ+LM, the exact complement of 2CQ+LP. These oligos were used in the mutagenesis reaction according to the manufacturer's protocol. Restriction enzyme analysis and DNA sequence analysis confirmed the insertion of the 9 nucleotide linker (GCGGCCGCC) between the C-terminus of phmGluR2//CaR and the N-terminus of $G\alpha_{q15}$. This construct was designated phmGluR2//CaR*AAA* $G\alpha_{q15}$.

B. Human GABA_BR2*AAA* $G\alpha_{q05}$ and human GABA_BR1a*AAA* $G\alpha_{q05}$

These constructs contain the human GABA_BR2 (hGABA_BR2: Genbank Accession # AJ 012188) and human GABA_BR1a (hGABA_BR1a: Genbank Accession # AJ 012185) fused at their C-terminus to the N-terminus of human $G\alpha_{q05}$ (h $G\alpha_{q05}$: Nature 363:274-276, 1993). Human GABA_BR2, hGABA_BR1a, and h $G\alpha_{q05}$ were cloned into the plasmid pcDNA3.1/Hygro+ (Invitrogen) and are designated phGABA_BR2,

phGABA_BR1a, and phGα_o5. The first reaction used two primers, XcmI-R2 (sense 20-mer, corresponding to nucleotides 2650-2669 of phGABA_BR2) and the hybrid primer R2/Go5(-) (antisense 45-mer, containing 18 nucleotides complementary to nucleotides 2806-2823 of phGABA_BR2 and 18 nucleotides complementary to nucleotides 1-18 of hGα_o5). These two complementary areas flank a 9 nucleotide sequence coding for 3 alanine sequences with a unique NotI restriction site. These primers were used to amplify a 200 base-pair PCR fragment.

In a separate PCR reaction, part of hGα_o5 was amplified using a hybrid primer R2/Gα_o5(+) (sense 45-mer), exactly complementary to R2/Go5(-) and XbaI-Go5 primer (22-mer containing 22 nucleotides complementary to nucleotides 873-895 of hGα_o5). These primers were used to amplify a 914 base-pair PCR product. The two PCR products generated from the above two reactions were annealed together in equimolar ratios in the presence of the external primers; XcmI-R2 and XbaI-Go5, and Pfu polymerase (Stratagene).

The resulting chimeric PCR product was digested with the restriction endonucleases XcmI and XbaI (New England Biolabs) and subcloned into phGABA_BR2 digested with the same two restriction enzymes. The resulting clone was then digested with HindIII and XbaI and subcloned into phGα_o5 cut with HindIII and XbaI resulting in the chimeric hGABA_BR*AAA*Gα_o5. The chimeric junction between the C-terminus hGABA_BR1a, the Ala linker, and the N-terminus of hGα_o5 was created using a recombinant PCR strategy similar to those described above.

To construct hGABA_BR1a*AAA*Gqo5, the first reaction used a commercially available T7 primer (Novagen) and the NtI hGBR1 primer (CAGAGTCATGGCGGCCGCCTTATAAAGCAAATGCACTCG) corresponding to nucleotide numbers 1-9 of hGα_o5 and nucleotide numbers 2863-2883 of hGABA_BR1a.

VIII. phmGluR8//CaR Construct

This chimera contains the extracellular and transmembrane domains of human mGluR8 linked to the intracellular cytoplasmic tail domain of the human CaR. The chimeric junction between hmGluR8 and the CaR was created using a recombinant PCR strategy

similar to those described above.

The first reaction used two primers, CH5A (sense 19-mer, corresponding to nucleotides 2187-2205 of human mGluR8, Stormann et al., International Publication Number WO97/48724) and the hybrid primer CH5B (antisense 40-mer, containing 22 nucleotides complementary to nucleotides 2523 - 2544 of human mGluR8, and 18 nucleotides complementary to nucleotides 2602-2619 of the human CaR). These primers were used to amplify a 375 bp PCR fragment of human mGluR8. In a separate PCR reaction using phCaR in the BlueScript SK(-) plasmid as template, a 750 bp fragment of the human CaR was amplified using a hybrid primer CH5C (sense 40-mer, exactly complementary to primer CH5B) and the T3 primer commercially available from Stratagene.

The two PCR products generated from the above two reactions were annealed together in equimolar ratios in the presence of the external primers CH5A and T3, and the Pfu DNA polymerase (Stratagene). The resulting chimeric PCR product was digested with BsrG I and Xba I (New England Biolabs) and subcloned into pmGluR8 digested with the same two restriction enzymes. The sequence of the resultant chimeric construct, pmGluR8//CaR, was verified by DNA sequence analysis.

IX. mGluR8//CaR*G α q15 Construct

This construct contains the hmGluR8//CaR chimeric receptor fused to human G α q15. The chimeric junction between the C-terminus of hmGluR8//CaR and the N-terminus of G α q15 was created using a recombinant PCR strategy similar to that described above for the construction of phmGluR2//CaR*G α q15.

The first reaction used two primers, CRP10A (sense 18-mer, corresponding to nucleotides 2812-2829 of phCaR) and the hybrid primer Gqi5/CaR (antisense 40-mer, containing 21 nucleotides complementary to nucleotides 3214-3234 phCaR, and 19 nucleotides complementary to nucleotides 1-19 of pG α q15). These primers were used to amplify a 441 bp PCR fragment of hmGluR8//CaR.

In a separate PCR reaction all of G α q15 was amplified using a hybrid primer CaR/Gqi5 (sense 40-mer, exactly complementary to primer Gqi5/CaR) and the Apa I-mut primer (20-mer). The two PCR products generated from the above two reactions were annealed

together in equimolar ratios in the presence of the external primers CRP10A and Apa I-mut, and the Pfu DNA polymerase (Stratagene).

The resulting chimeric PCR product was digested with BstE II and Apa I (New England Biolabs) and subcloned into pmGluR8//CaR digested with the same two restriction enzymes. The sequence of the resultant chimeric fusion construct, pmGluR8//CaR*G α _{q15}, was verified by DNA sequence analysis.

10 Example 2: Functional Expression of CaR/GABA_BR2

In vitro transcribed RNA (7 ng) encoding a chimeric CaR/GABA_BR2 (CaR extracellular and transmembrane domains, and intracellular GABA_BR2 domain) was co-injected with in vitro transcribed RNA (2 ng) encoding G α ₁₅ into *Xenopus* oocytes. Following a 72-hour incubation, the oocytes were voltage-clamped using standard electrophysiological techniques (Hille, B., Ionic Channels of Excitable Membranes, pp.30-33, Sinauer Associates, Inc., Sunderland, Ma., 1992). Activation of the chimeric receptor was detected by increases in the calcium-activated chloride current.

Application of the CaR activator 100 μ M Gd³⁺, resulted in reversible, oscillatory increases in the calcium-activated chloride current as shown in Figure 8. These data demonstrate the functional response of the chimeric CaR/GABA_BR2 receptor upon activation via a site within the CaR extracellular domain. In this assay, the G α ₁₅ subunit acts to promote signal transduction through intracellular pathways that mobilize intracellular Ca²⁺.

Example 3: Expression of Different G-Protein Fusion Receptors

30 The ability of different G-protein fusions to transduce signal resulting from ligand binding is shown in Figure 15. The different G-protein fusion receptors used in this example were as follows: mGluR2//CaR*G α _{q15} (SEQ. ID. NO. 37), CaR/mGluR2*G α _{q15} (SEQ. ID. NO. 33), and mGluR8//CaR*G α _{q15} SEQ. ID. NO. 41.

35 Oocytes suitable for injection were obtained from adult female *Xenopus laevis* toads using procedures described in C. J.

Marcus-Sekura and M. J. M. Hitchcock, Methods in Enzymology, Vol. 152 (1987).

Receptor fusion cRNAs were dissolved in water and 50 nl (12.5 ng/oocyte) were injected into individual oocytes.

5 Following injection, oocytes were incubated at 16°C in MBS containing 1 mM CaCl₂ for 2 to 7 days prior to electrophysiological recording.

Test substances were applied by superfusion at a flow rate of about 5 ml/min. Receptor fusion activation was determined by
10 measuring the increase in calcium-activated chloride current (I_{Cl}). Increases in I_{Cl} were quantified by measuring the peak inward current stimulated by activating agent, relative to the holding current at -60 mV. Application of 100 μM L-glutamate elicited a response from the mGluR2//CaR*Gαq15 and
15 mGluR8//CaR*Gαq15. Application of 100 μM Gd³⁺ activated the CaR/mGluR2*Gq15.

Other embodiments are within the following claims. Thus, while several embodiments have been shown and described, various
20 modifications may be made, without departing from the spirit and scope of the present invention.

Claims

1. A G-protein fusion receptor comprising
an extracellular domain comprising an extracellular domain
5 amino acid sequence substantially similar to either an
extracellular CaR amino acid sequence, an extracellular mGluR
amino acid sequence, or an extracellular GABA_B receptor amino acid
sequence;
a transmembrane domain joined to the carboxy terminus of
10 said extracellular domain, said transmembrane domain comprising a
transmembrane domain amino acid sequence substantially similar to
either a transmembrane CaR amino acid sequence, a transmembrane
mGluR amino acid sequence, or a transmembrane GABA_B receptor amino
acid sequence;
15 an intracellular domain joined to the carboxy terminus of
said transmembrane domain comprising all or a portion of an
intracellular amino acid sequence substantially similar to either
an intracellular CaR amino acid sequence, an intracellular mGluR
amino acid sequence, or an intracellular GABA_B receptor amino acid
20 sequence, provided that said portion is at least about 10 amino
acids;
an optionally present linker joined to the carboxy terminus
of said intracellular domain; and
a G-protein joined either to said intracellular domain or to
25 said optionally present linker, provided that said G-protein is
joined to said optionally present linker when said optionally
present linker is present.
2. The G-protein fusion receptor of claim 1, wherein said
30 extracellular domain consists of said extracellular domain amino
acid sequence, said transmembrane domain consists of said
transmembrane domain amino acid sequence; and said intracellular
domain consists of said transmembrane domain amino acid sequence.
- 35 3. The G-protein fusion receptor of claim 2, wherein said
optionally present linker is present and is a polypeptide 3 to 30
amino acids in length.

4. The G-prot in fusion receptor of claim 2, wherein said optionally present linker is not present.

5. The G-protein fusion receptor of claim 3 or 4, wherein
5 said G-protein is selected from the group consisting of: $G_{\alpha 15}$, $G_{\alpha 16}$, G_{qo5} , and G_{qi5}

6. The G-protein fusion of claim 5, wherein any of said
CaR sequence present is a human CaR sequence, any of said mGluR
10 sequence present is from a human mGluR, and any of said $GABA_B$
receptor sequence present is from human mGluR.

7. A nucleic acid comprising a nucleotide sequence
encoding for the G-protein fusion of any one of claims 1-6.
15

8. An expression vector comprising a nucleotide sequence
encoding for the G-protein fusion of any one of claims 1-6
transcriptionally coupled to a promoter.

9. A recombinant cell comprising the expression vector of
20 claim 8 and a cell wherein the G-protein fusion is expressed and
is functional.

10. A recombinant cell produced by combining a vector
25 comprising the nucleic acid of claim 9 and elements for
introducing heterologous nucleic acid into a cell wherein the G-
protein fusion receptor is expressed, and said cell.

11. A process for the production of a G-protein fusion
30 receptor comprising:
growing procaryotic or eukaryotic host cells comprising a
nucleic acid sequence expressing the G-protein fusion receptor of
any one of claims 1-6, under suitable nutrient conditions
allowing for cell growth.

35
12. A method of measuring the ability of a compound to
effect G-protein fusion activity comprising the steps of:

a) providing said compound to a cell expressing the G-
protein fusion receptor of any one of claims 1-6, and

b) measuring the ability of said compound to affect the activity of said receptor as an indication of the ability of said compound to effect G-protein fusion receptor activity.

- 5 13. A chimeric receptor comprising
 an extracellular domain comprising an extracellular domain
 amino acid sequence substantially similar to a sequence selected
 from the group consisting of SEQ ID NO: 1, SEQ ID NO: 2, SEQ ID
 NO: 3, SEQ ID NO: 4 and SEQ ID NO: 5;
10 a transmembrane domain comprising a transmembrane domain
 amino acid sequence substantially similar to a sequence selected
 from the group consisting of SEQ ID NO: 6, SEQ ID NO: 7, SEQ ID
 NO: 8, SEQ ID NO: 9, and SEQ ID NO: 10; and
 an intracellular cytoplasmic domain comprising an
15 intracellular domain amino acid sequence substantially similar to
 a sequence selected from the group consisting of SEQ ID NO: 11,
 SEQ ID NO: 12, SEQ ID NO: 13, and SEQ ID NO: 14;
 wherein at least one domain is present which comprises an
 amino acid sequence substantially similar to a sequence selected
20 from the group consisting of: SEQ ID NO: 2, SEQ ID NO: 3, SEQ ID
 NO: 4, SEQ ID NO: 7, SEQ ID NO: 8, and SEQ ID NO: 9, SEQ ID NO:
 12, SEQ ID NO: 13, and SEQ ID NO: 14; and at least one domain is
 present which comprises an amino acid sequence substantially
 similar to a sequence selected from the group consisting of: SEQ
25 ID NO: 1, SEQ ID NO: 5, SEQ ID NO: 6, SEQ ID NO: 10, SEQ ID NO:
 11, and SEQ ID NO: 15.

14. The chimeric receptor of claim 13 wherein said
 extracellular domain has a sequence similarity of at least 90%
30 with an amino acid sequence selected from the group consisting of
 SEQ ID NOs: 2, 3, and 4; said transmembrane domain has a sequence
 similarity of at least 90% with an amino acid sequence selected
 from the group consisting of SEQ ID Nos: 6, 7, 8, 9, and 10; and
 said intracellular domain has a sequence similarity of at least
35 90% with an amino acid sequence selected from the group
 consisting of SEQ ID NOs: 11 and 15.

15. The chimeric receptor of claim 14, wherein said
 extracellular domain has a sequence similarity of at least 90%

with the amino acid sequence of SEQ ID NO: 2; said transmembrane domain has a sequence similarity of at least 90% with the amino acid sequence SEQ ID NO: 7; and said intracellular domain has a sequence similarity of at least 90% with the amino acid sequence of SEQ ID NO: 11.

16. The chimeric receptor of claim 14, wherein said extracellular domain has a sequence similarity of at least 90% with the amino acid sequence of SEQ ID NO: 3; said transmembrane domain has a sequence similarity of at least 90% with the amino acid sequence of SEQ ID NO: 8; and said intracellular domain has a sequence similarity of at least 90% with the amino acid sequence of SEQ ID NO 11.

17. The chimeric receptor of claim 14, wherein said extracellular domain has a sequence similarity of at least 90% with the amino acid sequence SEQ ID NO: 4; said transmembrane domain has a sequence similarity of at least 90% with the amino acid sequence of SEQ ID NO: 9; and said intracellular domain has a sequence similarity of at least 90% with the amino acid sequence of SEQ ID NO 11.

18. The chimeric receptor of claim 13, wherein said extracellular domain has a sequence similarity of at least 90% with an amino acid sequence selected from the group consisting of SEQ ID NOS: 1, 2, 3, 4 and 5; said transmembrane domain has a sequence similarity of at least 90% with an amino acid sequence selected from the group consisting of SEQ ID Nos: 7, 8, and 9; and said intracellular domain has a sequence similarity of at least 90% with an amino acid sequence selected from the group consisting of SEQ ID NOS: 11, 12, 13, 14, and 15.

19. The chimeric receptor of claim 18, wherein said extracellular domain has a sequence similarity of at least 90% with the amino acid sequence of SEQ ID NO: 1; said transmembrane domain has a sequence similarity of at least 90% with the amino acid sequence of SEQ ID NO: 7; and said intracellular domain has a sequence similarity of at least 90% with the amino acid sequence of SEQ ID NO: 11.

20. The chimeric receptor of claim 18, wherein said extracellular domain has a sequence similarity of at least 90% with the amino acid sequence of SEQ ID NO: 1; said transmembrane domain has a sequence similarity of at least 90% with the amino acid sequence of SEQ ID NO: 8; and said intracellular domain has a sequence similarity of at least 90% with the amino acid sequence of SEQ ID NO 11.

21. The chimeric receptor of claim 18, wherein said extracellular domain has a sequence similarity of at least 90% with the amino acid sequence of SEQ ID NO: 1; said transmembrane domain has a sequence similarity of at least 90% with the amino acid sequence of SEQ ID NO: 9; and said intracellular domain has a sequence similarity of at least 90% with the amino acid sequence of SEQ ID NO 11.

22. The chimeric receptor of claim 13, wherein said extracellular domain has a sequence similarity of at least 90% with an amino acid sequence selected from the group consisting of SEQ ID NOS: 1, 2, 3, 4, and 5; said transmembrane domain has a sequence similarity of at least 90% with an amino acid sequence selected from the group consisting of SEQ ID Nos: 6, 7, 8, 9, and 10; and said intracellular domain has a sequence similarity of at least 90% with an amino acid sequence selected from the group consisting of SEQ ID NOS: 12, 13, and 14.

23. The chimeric receptor of claim 22, wherein said extracellular domain has a sequence similarity of at least 90% with the amino acid sequence of SEQ ID NO: 1; said transmembrane domain has a sequence similarity of at least 90% with the amino acid sequence of SEQ ID NO: 6; and said intracellular domain has a sequence similarity of at least 90% with the amino acid sequence of SEQ ID NO: 12.

24. The chimeric receptor of claim 22, wherein said extracellular domain has a sequence similarity of at least 90% with the amino acid sequence of SEQ ID NO: 1; said transmembrane domain has a sequence similarity of at least 90% with the amino

acid sequence of SEQ ID NO: 7; and said intracellular domain has a sequence similarity of at least 90% with the amino acid sequence of SEQ ID NO: 12.

5 25. The chimeric receptor of claim 22, wherein said extracellular domain has a sequence similarity of at least 90% with the amino acid sequence of SEQ ID NO: 1; said transmembrane domain has a sequence similarity of at least 90% with the amino acid sequence of SEQ ID NO: 8; and said intracellular domain has
10 a sequence similarity of at least 90% with the amino acid sequence of SEQ ID NO: 13.

 26. The chimeric receptor of claim 22, wherein said extracellular domain has a sequence similarity of at least 90%
15 with the amino acid sequence of SEQ ID NO: 1; said transmembrane domain has a sequence similarity of at least 90% with the amino acid sequence of SEQ ID NO: 6; and said intracellular domain has a sequence similarity of at least 90% with the amino acid sequence of SEQ ID NO: 13.

20 27. The chimeric receptor of claim 22, wherein said extracellular domain has a sequence similarity of at least 90% with the amino acid sequence of SEQ ID NO: 1; said transmembrane domain has a sequence similarity of at least 90% with the amino
25 acid sequence of SEQ ID NO: 9; and said intracellular domain has a sequence similarity of at least 90% with the amino acid sequence of SEQ ID NO: 14.

 28. The chimeric receptor of claim 22, wherein said
30 extracellular domain has a sequence similarity of at least 90% with the amino acid sequence of SEQ ID NO: 1; said transmembrane domain has a sequence similarity of at least 90% with the amino acid sequence of SEQ ID NO: 6; and said intracellular domain has a sequence similarity of at least 90% with the amino acid
35 sequence of SEQ ID NO: 14.

 29. The chimeric receptor of any one of claims 13-28, wherein said receptor functional couples to a G-protein.

30. The chimeric receptor of any one of claims 13-28, wherein said chimeric receptor consists of said extracellular domain, said transmembrane domain, said intracellular domain, and an optionally present G-protein α subunit covalently joined to said intracellular domain.

31. The chimeric receptor of claim 30, wherein said chimeric receptor consists of said extracellular domain, said transmembrane domain, and said intracellular domain.

32. The chimeric receptor of claim 30, wherein said G-protein α subunit consists of the amino acid sequence of SEQ ID Nos: 16 or 17.

33. A nucleic acid comprising a nucleotide sequence encoding for the chimeric receptor of any one of claims 13-32.

34. An expression vector comprising a nucleotide sequence encoding for the chimeric receptor of any one of claims 13-32 transcriptionally coupled to a promoter.

35. A recombinant cell comprising the expression vector of claim 34 and a cell wherein the chimeric receptor is expressed and is functional.

36. A recombinant cell produced by combining a vector comprising the nucleic acid of claim 33 and elements for introducing heterologous nucleic acid into a cell wherein the chimeric receptor is expressed, and said cell.

37. A process for the production of a chimeric receptor comprising:
growing procaryotic or eukaryotic host cells comprising a nucleic acid sequence expressing the chimeric receptor of any one of claims 13-32, under suitable nutrient conditions allowing for cell growth.

38. A method of measuring the ability of a compound to effect GABA_BR or mGluR activity comprising the steps of:

a) providing said compound to a cell expressing the chimeric receptor of any one of claims 13-32, and

b) measuring the ability of said compound to affect the activity of said receptor as an indication of the ability of said compound to effect GABA_AR or mGluR activity.

39. The method of claim 38, wherein said method measures activity at a GABA_AR.

40. The method of claim 38, wherein said method measures activity at a mGluR.

41. A fusion receptor polypeptide comprising a receptor and a G-protein α subunit, wherein said G-protein α subunit is fused to the intracellular domain of said receptor, provided that said receptor is not an adrenoceptor.

I/III

ClustalW Formatted Alignments

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SEQ ID 1 M A F Y S C C W V L L A L T W H T S A Y G P D Q R
SEQ ID 2 M L L L L L L A P L F L R P P G A G G A Q T P N A
SEQ ID 3 M G P G A P F A R V G W P L P L L V V M A A G V A
SEQ ID 4 M A S P R S S G Q P G P X P P P P P P A R L L L
SEQ ID 5 M V C E G K R S A S C P C F F L L T A K F Y W I L

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SEQ ID 1 A Q K K G D I I L G G L F P I H F G V A A K D Q D
SEQ ID 2 T S E G C Q I I H P P W E G G I R Y R G L T R D Q
SEQ ID 3 P V W A S H S P H L P R P H S R V P P H P S S E R
SEQ ID 4 L L L L P L L L P L A P G A W G W A R G A P R P P
SEQ ID 5 T M M Q R T H S Q E Y A H S I R V D G D I I L G G

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SEQ ID 1 L K S R P E S V E C I R Y N F R G F R W L Q A M I
SEQ ID 2 V K A I N F L P V D Y E I E Y V C R G E R E V V G
SEQ ID 3 R A V Y I G A L F P M S G G W P G G Q A C Q P A V
SEQ ID 4 P S S P P L S I M G L M P L T K E V A K G S I G R
SEQ ID 5 L F P V H A K G E R G V P C G E L K K E K G I H R

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SEQ ID 1 F A I E E I N S S P A L L P N L T L G Y R I F D T
SEQ ID 2 P K V R K C L A N G S W T D M D T P S R C V R I C
SEQ ID 3 E M A L E D V N S R R D I L P D Y E L K L I H H D
SEQ ID 4 G V L P A V E L A I E Q I R N E S L L R P Y F L D
SEQ ID 5 L E A M L Y A I D Q I N K D P D L L S N I T L G V

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SEQ ID 1 C N T V S K A L E A T L S F V A Q N K I D S L N L
SEQ ID 2 S K S Y L T L E N G K V F L T G G D L P A L D G A
SEQ ID 3 S K C D P G Q A T K Y L Y E L L Y N D P I K I I L
SEQ ID 4 L R L Y D T E C D N A K G L K A F Y D A I K Y G P
SEQ ID 5 R I L D T C S R D T Y A L E Q S L T F V Q A L I E

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SEQ ID 1 D E F C N C S E H I P S T I A V V G A T G S G V S
SEQ ID 2 R V D F R C D P D F H L V G S S R S I C S Q G Q W
SEQ ID 3 M P G C S S V S T L V A E A A R M W N L I V L S Y
SEQ ID 4 N H L M V F G G V C P S V T S I I A E S L Q G W N
SEQ ID 5 K D A S D V K C A N G D P P I F T K P D K I S G V

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SEQ ID 1 T A V A N L L G L F Y I P Q V S Y A S S S R L L S
SEQ ID 2 S T P K P H C Q V N R T P H S E R R A V Y I G A L
SEQ ID 3 G S S S P A L S N R Q R F P T F F R T H P S A T L
SEQ ID 4 L V Q L S F A A T T P V L A D K K K Y P Y F F R T
SEQ ID 5 I G A A A S S V S I M V A N I L R L F K I P Q I S

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FIG. 1a.

2/111

SEQ ID 1 NKNQFKSFLRTIPNDEHQATAMADI
 SEQ ID 2 FPMSSGGWPGGQACQPAVEMALEDVN
 SEQ ID 3 HNPTRVKLF EKWGWKKIATIQQTTE
 SEQ ID 4 VPSDNAVNPAILKLLKHYQWKR VGT
 SEQ ID 5 YASTAPELS DNTRYDFFSRVVPDS

SEQ ID 1 IEYFRWNWVG TIAADDDYGRPGIEK
 SEQ ID 2 SRRDILPDYELKLIHHDSKCDPGQA
 SEQ ID 3 VFTSTLDDLEERVKEAGIEITFRQS
 SEQ ID 4 LTQDVQRFSEVRNDLTGVLYGEDIE
 SEQ ID 5 YQAQAMVDIVTALGWNYVSTLASEG

SEQ ID 1 FREEAEERD ICIDFSELISQYSDEE
 SEQ ID 2 TKYLYELLYNDPIKILMPGCSSVS
 SEQ ID 3 FFS DPAVPVKNLKRQDARIIVGLFY
 SEQ ID 4 ISDTESFSNDPCTSVKKLKGNDVRI
 SEQ ID 5 NYGESGVEAFTQISREIGGVCI AQ S

SEQ ID 1 EIQHVVEVIQNSTAKVIVVFSSGPD
 SEQ ID 2 TLVAEAARMWN LIVLSYGSSSPALS
 SEQ ID 3 ETEARKVFCEVYKERLFGKKYVWFL
 SEQ ID 4 ILGQFDQNM AAKVFCCAYEENMYGS
 SEQ ID 5 QKIPREPRPGEF EKIIKRLLET PNA

SEQ ID 1 LEPLIKEIVRRNITGKIWLASEAWA
 SEQ ID 2 NRQRFPTFFRTHPSATLHNPTRVKL
 SEQ ID 3 IGWYADNWFKIYDPSINCTVDEMTE
 SEQ ID 4 KYQWIIPGWYEPSWWEQVHTEANSS
 SEQ ID 5 RAVIMFANEDDIRRILEAAKKLNQS

SEQ ID 1 SSSLIAMPPQYFHVVG GTIGFALKAG
 SEQ ID 2 FEKWWGKKIATIQQTTEVFTSTLDD
 SEQ ID 3 AVEGHITTEIVMLNPANTRSI SNMT
 SEQ ID 4 RCLRKNNLLAAMEGYIGVDFEPLSSK
 SEQ ID 5 GHFLWIGSDSWGSKIAPVYQQEEIA

SEQ ID 1 QIPGFREFLKKVHPRKSVHNGFAKE
 SEQ ID 2 LEERVKEAGIEITFRQSFFSDPAVP
 SEQ ID 3 SQEFVEKLT KRLKRHP EETGGFQEA
 SEQ ID 4 QIKTISGKTPQQYEREYNNKRSGVG
 SEQ ID 5 EGAVTILPKRASIDGFDRYFRSRTL

FIG. 1b.

3/III

SEQ ID 1 FWEETFNCHLQEGAKGPLPVDTF LR
 SEQ ID 2 VKNLKRQDARIIVGLFYETEARKVF
 SEQ ID 3 PLAYDAIWALALALNKTSGGGGRSG
 SEQ ID 4 PSKFHGYAYDGIWVIAKT LQRAMET
 SEQ ID 5 ANNRRNVWF AEFWEENFGCKLGSHG

SEQ ID 1 GHEESGDRFSNSSTA FRPLCTGDEN
 SEQ ID 2 CEVYKERLFGKKYVWFLIGWYADNW
 SEQ ID 3 VRLED FNYNNQTITDQIYRAMNSSS
 SEQ ID 4 LHASSRHQRIQDFNYTDHTLGR IIL
 SEQ ID 5 KRNSHIKKCTGLERIARDSSSYEQEG

SEQ ID 1 ISSVETPYIDYTHLRISYNVYLAVY
 SEQ ID 2 FKIYDPSINCTVDEMTEAVEGHITT
 SEQ ID 3 FEGVSGHVVFDA S GSRMAWTLIEQL
 SEQ ID 4 NAMNETNFFFGVTGQVVFRNGERMGT
 SEQ ID 5 KVQFVIDAVYSMAYALHNMHKDLC P

SEQ ID 1 SIAHALQDIYTCLPGRGLFTNGSCA
 SEQ ID 2 EIVMLNPANTRSISNMTS QEFVEKL
 SEQ ID 3 QGGSYKKIGYYDSTKDDL SWSKTDK
 SEQ ID 4 IKFTQFQDSREVKVGEYNAVADTLE
 SEQ ID 5 GYIGLCPRMSTIDGKELLGYIRAVN

SEQ ID 1 DIKKVEAWQV LKHLRHLNFTNNMGE
 SEQ ID 2 TKRLKRHP EETGGFQEAPLAYDAIW
 SEQ ID 3 WIGGSPPADQTLVIKTFRFLSQK
 SEQ ID 4 IINDTIRFQGS EPPKDKTIILEQLR
 SEQ ID 5 FNGSAGTPVTFNENGDA PGRYDIFQ

SEQ ID 1 QVTFDEC GDLVGNYSIINWHLSPED
 SEQ ID 2 ALALALNKTSGGGGRSGVRLED FNY
 SEQ ID 3
 SEQ ID 4 KISLP
 SEQ ID 5 YQITNKSTEYKVIGHWTNQLHLKVE

SEQ ID 1 GSIVFKEVGYYNVYAKKGERLFINE
 SEQ ID 2 NNQTITDQIYRAMNSSS SFEGVSGHV
 SEQ ID 3
 SEQ ID 4
 SEQ ID 5 DMQWAHREH THPASVCSLPCKPGER

FIG. 1c.

4/III

SEQ ID 1 E K I L W S G F S R E V P F S N C S R D C L A G T
SEQ ID 2 V F D A S G S R M A W T L I E Q L Q G G S Y K K I
SEQ ID 3
SEQ ID 4
SEQ ID 5 K K T V K G V P C C W H C E R C E G Y N Y Q V D E

SEQ ID 1 R K G I I E G E P T C C F E C V E C P D G E Y S D
SEQ ID 2 G Y Y D S T K D D L S W S K T D K W I G G S P P A
SEQ ID 3
SEQ ID 4
SEQ ID 5 L S C E L C P L D Q R P N M N R T G C Q L I P I I

SEQ ID 1 E T D A S A C N K C P D D F W S N E N H T S C I A
SEQ ID 2 D Q T L V I K T F R F L S Q K
SEQ ID 3
SEQ ID 4
SEQ ID 5 K L E W H S P W

SEQ ID 1 K E I E F L S W T E P F
SEQ ID 2
SEQ ID 3
SEQ ID 4
SEQ ID 5

FIG. 1d.

5/III

SEQ ID 6 G I A L T L F A V L G I F L T A F V L G V F I K F R N T P I
 SEQ ID 7 L F I S V S V L S S L G I V L A V V C L S F N I Y N S H V R
 SEQ ID 8 L F I S V S V L S S L G I V L A V V C L S F N I Y N S H V R
 SEQ ID 9 L Y S I L S A L T I L G M I M A S A F L F F N I K N R N Q K
 SEQ ID 10 A V V P V F V A I L G I I A T T F V I V T F V R Y N D T P I

SEQ ID 6 V K A T N R E L S Y L L L F S L L C C F S S S L F F I G E P
 SEQ ID 7 Y I Q N S Q P N L N N L T A V G C S L A L A A V F P L G L D
 SEQ ID 8 Y I Q N S Q P N L N N L T A V G C S L A L A A V F P L G L D
 SEQ ID 9 L I K M S S P Y M N N L I I L G G M L S Y A S I F L F G L D
 SEQ ID 10 V R A S G R E L S Y V L L T G I F L C Y S I T F L M I A A P

SEQ ID 6 Q D W T C R L R Q P A F G I S F V L C I S C I L V K T N R V
 SEQ ID 7 G Y H I G R N Q F P F V C Q A R L W L L G L G F S L G Y G S
 SEQ ID 8 G Y H I G R N Q F P F V C Q A R L W L L G L G F S L G Y G S
 SEQ ID 9 G S F V S E K T F E T L C T V R T W I L T V G Y T T A F G A
 SEQ ID 10 D T I I C S F R R V F L G L G M C F S Y A A L L T K T N R I

SEQ ID 6 L L V F E A K I P T S F H R K W W G L N L Q F L L V F L C T
 SEQ ID 7 M F T K I W W V H T V F T K K E E K K E W R K T L E P W K L
 SEQ ID 8 M F T K I W W V H T V F T K K E E K K E W R K T L E P W K L
 SEQ ID 9 M F A K T W R V H A I F K N V K M K K K I I K D Q K L L V I
 SEQ ID 10 H R I F E Q G K K S V T A P K F I S P A S Q L V I T F S L I

SEQ ID 6 F M Q I V I C V I W L Y T A P P S S Y R N Q E L E D E I I F
 SEQ ID 7 Y A T V G L L V G M D V L T L A I W Q I V D P L H R T I E T
 SEQ ID 8 Y A T V G L L V G M D V L T L A I W Q I V D P L H R T I E T
 SEQ ID 9 V G G M L L I D L C I L I C W Q A V D P L R R T V E K Y S M
 SEQ ID 10 S V Q L L G V F V W F V V D P P H I I I D Y G E Q R T L D P

SEQ ID 6 I T C H E G S L M A L G F L I G Y T C L L A A I C F F F A F
 SEQ ID 7 F A K E E P K E D I D V S I L P Q L E H C S S R K M N T W L
 SEQ ID 8 F A K E E P K E D I D V S I L P Q L E H C S S R K M N T W L
 SEQ ID 9 E P D P A G R D I S I R P L L E H C E N T H M T I W L G I V
 SEQ ID 10 E K A R G V L K C D I S D L S L I C S L G Y S I L L M V T C

SEQ ID 6 K S R K L P E N F N E A K F I T F S M L I F F I V W I S F I
 SEQ ID 7 G I F Y G Y K G L L L L L G I F L A Y E T K S V S T E K I N
 SEQ ID 8 G I F Y G Y K G L L L L L G I F L A Y E T K S V S T E K I N
 SEQ ID 9 Y A Y K G L L M L F G C F L A W E T R N V S I P A L N D S K
 SEQ ID 10 T V Y A I K T R G V P E T F N E A K P I G F T M Y T T C I I

FIG. 2a.

6/III

SEQ ID 6 P A Y A S T Y G K F V S A V E V I A I L A A S F G L L A C I
SEQ ID 7 D H R A V G M A I Y N V A V L C L I T A P V T M I L S S Q Q
SEQ ID 8 D H R A V G M A I Y N V A V L C L I T A P V T M I L S S Q Q
SEQ ID 9 Y I G M S V Y N V G I M C I I G A A V S F L T R D Q P N V Q
SEQ ID 10 W L A F I P I F F G T A Q S A E K M Y I Q T T T L T V S M S

SEQ ID 6 F F N K I Y I I L F
SEQ ID 7 D A A F A F A S L A I V F S S Y I T L V V L F V P K M
SEQ ID 8 D A A F A F A S L A I V F S S Y I T L V V L F V P K M
SEQ ID 9 F C I V A L V I I F C S T I T L C L V F V P K L
SEQ ID 10 L S A S V S L G M L Y M P K V Y I I I F

FIG. 2b.

7/III

SEQ ID 11 K P S R N T I E E V R C S T A A H A F K V A A R A T L R R S
 SEQ ID 12 R R L I T R G E W Q S E A Q D T M K T G S S T N N N E E E K
 SEQ ID 13 R R L I T R G E W Q S E A Q D T M K T G S S T N N N E E E K
 SEQ ID 14 I T L R T N P D A A T Q N R R F Q F T Q N Q K K E D S K T S
 SEQ ID 15 H P E Q N V Q K R K R S F K A V V T A A T M Q S K L I Q K G

SEQ ID 11 N V S R K R S S S L G G S T G S T P S S S I S S K S N S E D
 SEQ ID 12 S R L L E K E N R E L E K I I A E K E E R V S E L R H Q L Q
 SEQ ID 13 S R L L E K E N R E L E K I I A E K E E R V S E L R H Q L Q
 SEQ ID 14 T S V T S V N Q A S T S R L E G L Q S E N H R L R M K I T E
 SEQ ID 15 N D R P N G E V K S E L C E S L E T N S K S S V E F P M V K

SEQ ID 11 P F P Q P E R Q K Q Q Q P L A L T Q Q E Q Q Q Q P L T L P Q
 SEQ ID 12 S R Q Q L R S R R H P P T P P E P S G G L P R G P P E P P D
 SEQ ID 13 S R Q Q L R S R R H P P T P P E P S G G L P R G P P E P P D
 SEQ ID 14 L D K D L E E V T M Q L Q D T P E K T T Y I K Q N H Y Q E L
 SEQ ID 15 S G S T S

SEQ ID 11 Q Q R S Q Q Q P R C K Q K V I F G S G T V T F S L S F D E P
 SEQ ID 12 R L S C D G S R V H L L Y K
 SEQ ID 13 R L S C D G S R V H L L Y K
 SEQ ID 14 N D I L N L G N F T E S T D G G K A I L K N H L D Q N P Q L
 SEQ ID 15

SEQ ID 11 Q K N A M A H G N S T H Q N S L E A Q K S S D T L T R H Q P
 SEQ ID 12
 SEQ ID 13
 SEQ ID 14 Q W N T T E P S R T C K D P I E D I N S P E H I Q R R L S L
 SEQ ID 15

SEQ ID 11 L L P L Q C G E T D L D L T V Q E T G L Q G P V G G D Q R P
 SEQ ID 12
 SEQ ID 13
 SEQ ID 14 Q L P I L H H A Y L P S I G G V D A S C V S P C V S P T A S
 SEQ ID 15

SEQ ID 11 E V E D P E E L S P A L V V S S S Q S F V I S G G G S T V T
 SEQ ID 12
 SEQ ID 13
 SEQ ID 14 P R H R H V P P S F R V M V S G L
 SEQ ID 15

FIG. 3a.

8/III

SEQ ID 11 E N V V N S
SEQ ID 12
SEQ ID 13
SEQ ID 14
SEQ ID 15

FIG. 3b.

9/III

SEQ. ID. NO. 16 M A R S L T W G C C P W C L T E E E K T A A R I D Q E I N R
 SEQ. ID. NO. 17 M A R S L T W R C C P W C L T E D E K A A A R V D Q E I N R

SEQ. ID. NO. 16 I L L E Q K K Q E R E E L K L L L L G P G E S G K S T F I K
 SEQ. ID. NO. 17 I L L E Q K K Q D R G E L K L L L L G P G E S G K S T F I K

SEQ. ID. NO. 16 Q M R I I H G V G Y S E E D R R A F R L L I Y Q N I F V S M
 SEQ. ID. NO. 17 Q M R I I H G A G Y S E E E R K G F R P L V Y Q N I F V S M

SEQ. ID. NO. 16 Q A M I D A M D R L Q I P F S R P D S K Q H A S L V M T O D
 SEQ. ID. NO. 17 R A M I E A M E R L Q I P F S R P E S K H H A S L V M S O D

SEQ. ID. NO. 16 P Y K V S T F E K P Y A V A M Q Y L W R D A G I R A C Y E R
 SEQ. ID. NO. 17 P Y K V T T F E K R Y A A A M Q W L W R D A G I R A C Y E R

SEQ. ID. NO. 16 R R E F H L L D S A V Y Y L S H L E R I S E D S Y I P T A Q
 SEQ. ID. NO. 17 R R E F H L L D S A V Y Y L S H L E R I T E E G Y V P T A Q

SEQ. ID. NO. 16 D V L R S R M P T T G I N E Y C F S V K K T K L R I V D V G
 SEQ. ID. NO. 17 D V L R S R M P T T G I N E Y C F S V Q K T N L R I V D V G

SEQ. ID. NO. 16 G Q R S E R R K W I H C F E N V I A L I Y L A S L S E Y D O
 SEQ. ID. NO. 17 G Q K S E R K K W I H C F E N V I A L I Y L A S L S E Y D O

SEQ. ID. NO. 16 C L E E N D Q E N R M E E S L A L F S T I L E L P W F K S T
 SEQ. ID. NO. 17 C L E E N N Q E N R M K E S L A L F G T I L E L P W F K S T

SEQ. ID. NO. 16 S V I L F L N K T D I L E D K I H T S H L A T Y F P S F Q G
 SEQ. ID. NO. 17 S V I L F L N K T D I L E E K I P T S H L A T Y F P S F Q G

SEQ. ID. NO. 16 P R R D A E A A K S F I L D M Y A R V Y A S C A E P Q D G G
 SEQ. ID. NO. 17 P K Q D A E A A K R F I L D M Y T R M Y T G C V D G P E G S

SEQ. ID. NO. 16 R K G S R A R R F F A H F T C A T D T Q S V R S V F K D V R
 SEQ. ID. NO. 17 K K G A R S R R L F S H Y T C A T D T Q N I R K V F K D V R

FIG. 4a.

10/III

SEQ. ID. NO. 16 D S V L A R Y L D E I N L L
SEQ. ID. NO. 17 D S V L A R Y L D E I N L L

FIG. 4b.

II/III

ClustalW Formatted Alignments

SEQ. ID. NO. 18 A T G G C A T T T T A T A G C T G C T G C T G G G
 SEQ. ID. NO. 19 A T G T T G C T G C T G C T G C T A C T G G C G C
 SEQ. ID. NO. 20 A T G G G G C C C G G G G C C C C T T T T G C C C
 SEQ. ID. NO. 21 A T G G C T T C C C C G C G G A G C T C C G G G C

SEQ. ID. NO. 18 T C C T C T T G G C A C T C A C C T G G C A C A C
 SEQ. ID. NO. 19 C A C T C T T C C T C C G C C C C C C G G G C G C
 SEQ. ID. NO. 20 G G G T G G G G T G G C C A C T G C C G C T T C T
 SEQ. ID. NO. 21 A G C C C G G G C C G C - G C C G C C G C C G C C

SEQ. ID. NO. 18 C T C T G C C T A C G G G C C A G A C C A G C G A
 SEQ. ID. NO. 19 G G G C G G G G C G C A G A C C C C C A A C G C C
 SEQ. ID. NO. 20 G G T T G T G A T G G C G G C A G G G G T G G C T
 SEQ. ID. NO. 21 A C C G C C G C C C G C G C G C C T G C T A C T G

SEQ. ID. NO. 18 G C C C A A A A G A A G G G G G A C A T T A T C C
 SEQ. ID. NO. 19 A C C T C A G A A G G T T G C C A G A T C A T A C
 SEQ. ID. NO. 20 C C G G T G T G G G C C T C C C A C T C C C C C C
 SEQ. ID. NO. 21 C T A C T G C T G C T G C C G C T G C T G C T G C

SEQ. ID. NO. 18 T T G G G G G G C T C T T T C C T A T T C A T T T
 SEQ. ID. NO. 19 A C C C G C C C T G G G A A G G G G G C A T C A G
 SEQ. ID. NO. 20 A T C T C C C G C G G C C T C A C T C G C G G G T
 SEQ. ID. NO. 21 C T C T G G C G C C C G G G G C C T G G G G C T G

SEQ. ID. NO. 18 T G G A G T A G C A G C T A A A G A T C A A G A T
 SEQ. ID. NO. 19 G T A C C G G G G C C T G A C T C G G G A C C A G
 SEQ. ID. NO. 20 C C C C C G C A C C C C T C C T C A G A A C G G
 SEQ. ID. NO. 21 G G C G C G G G G C G C C C C C C G G C C G C C G

SEQ. ID. NO. 18 C T C A A A T C A A G G C C G G A G T C T G T G G
 SEQ. ID. NO. 19 G T G A A G G C T A T C A A C T T C C T G C C A G
 SEQ. ID. NO. 20 C G C G C A G T G T A C A T C G G G G C A C T G T
 SEQ. ID. NO. 21 C C C A G C A G C C C G C C G C T C T C C A T C A

SEQ. ID. NO. 18 A A T G T A T C A G G T A T A A T T T C C G T G G
 SEQ. ID. NO. 19 T G G A C T A T G A G A T T G A G T A T G T G T G
 SEQ. ID. NO. 20 T T C C C A T G A G C G G G G G C T G G C C A G G
 SEQ. ID. NO. 21 T G G G C C T C A T G C C G C T C A C C A A G G A

FIG. 5a.

12/III

SEQ. ID. NO. 18 G T T T C G C T G G T T A C A G G C T A T G A T A
SEQ. ID. NO. 19 C C G G G G G G A G C G C G A G G T G G T G G G G
SEQ. ID. NO. 20 G G G C C A G G C C T G C C A G C C C G C G G T G
SEQ. ID. NO. 21 G G T G G C C A A G G G C A G C A T C G G G C G C

SEQ. ID. NO. 18 T T T G C C A T A G A G G A G A T A A A C A G C A
SEQ. ID. NO. 19 C C C A A G G T C C G C A A G T G C C T G G C C A
SEQ. ID. NO. 20 G A G A T G G C G C T G G A G G A C G T G A A T A
SEQ. ID. NO. 21 G G T G T G C T C C C C G C C G T G G A A C T G G

SEQ. ID. NO. 18 G C C C A G C C C T T C T T C C C A A C T T G A C
SEQ. ID. NO. 19 A C G G C T C C T G G A C A G A T A T G G A C A C
SEQ. ID. NO. 20 G C C G C A G G G A C A T C C T G C C G G A C T A
SEQ. ID. NO. 21 C C A T C G A G C A G A T C C G C A A C G A G T C

SEQ. ID. NO. 18 G C T G G G A T A C A G G A T A T T T G A C A C T
SEQ. ID. NO. 19 A C C C A G C C G C T G T G T C C G A A T C T G C
SEQ. ID. NO. 20 T G A G C T C A A G C T C A T C C A C C A C G A C
SEQ. ID. NO. 21 A C T C C T G C G C C C C T A C T T C C T C G A C

SEQ. ID. NO. 18 T G C A A C A C C G T T T C T A A G G C C T T G G
SEQ. ID. NO. 19 T C C A A G T C T T A T T T G A C C C T G G A A A
SEQ. ID. NO. 20 A G C A A G T G T G A T C C A G G C C A A G C C A
SEQ. ID. NO. 21 C T G C G G C T C T A T G A C A C G G A G T G C G

SEQ. ID. NO. 18 A A G C C A C C C T G A G T T T T G T T G C T C A
SEQ. ID. NO. 19 A T G G G A A G G T T T T C C T G A C G G G T G G
SEQ. ID. NO. 20 C C A A G T A C C T A T A T G A G C T G C T C T A
SEQ. ID. NO. 21 A C A A C G C A A A A G G G T T G A A A G C C T T

SEQ. ID. NO. 18 A A A C A A A A T T G A T T C T T T G A A C C T T
SEQ. ID. NO. 19 G G A C C T C C C A G C T C T G G A C G G A G C C
SEQ. ID. NO. 20 C A A C G A C C C T A T C A A G A T C A T C C T T
SEQ. ID. NO. 21 C T A C G A T G C A A T A A A A T A C G G G C C G

SEQ. ID. NO. 18 G A T G A G T T C T G C A A C T G C T C A G A G C
SEQ. ID. NO. 19 C G G G T G G A T T T C C G G T G T G A C C C C G
SEQ. ID. NO. 20 A T G C C T G G C T G C A G C T C T G T C T C C A
SEQ. ID. NO. 21 A A C C A C T T G A T G G T G T T T G G A G G C G

FIG. 5b.

13/III

SEQ. ID. NO. 18 A C A T T C C C T C T A C G A T T G C T G T G G T
SEQ. ID. NO. 19 A C T T C C A T C T G G T G G G C A G C T C C C G
SEQ. ID. NO. 20 C G C T G G T G G C T G A G G C T G C T A G G A T
SEQ. ID. NO. 21 T C T G T C C A T C C G T C A C A T C C A T C A T

SEQ. ID. NO. 18 G G G A G C A A C T G G C T C A G G C G T C T C C
SEQ. ID. NO. 19 G A G C A T C T G T A G T C A G G G C C A G T G G
SEQ. ID. NO. 20 G T G G A A C C T C A T T G T G C T T T C C T A T
SEQ. ID. NO. 21 T G C A G A G T C C C T C C A A G G C T G G A A T

SEQ. ID. NO. 18 A C G G C A G T G G C A A A T C T G C T G G G G C
SEQ. ID. NO. 19 A G C A C C C C C A A G C C C C A C T G C C A G G
SEQ. ID. NO. 20 G G C T C C A G C T C A C C A G C C C T G T C A A
SEQ. ID. NO. 21 C T G G T G C A G C T T T C T T T T G C T G C A A

SEQ. ID. NO. 18 T C T T C T A C A T T C C C C A G G T C A G T T A
SEQ. ID. NO. 19 T G A A T C G A A C G C C A C A C T C A G A A C G
SEQ. ID. NO. 20 A C C G G C A G C G T T T C C C C A C T T T C T T
SEQ. ID. NO. 21 C C A C G C C T G T T C T A G C C G A T A A G A A

SEQ. ID. NO. 18 T G C C T C C T C C A G C A G A C T C C T C A G C
SEQ. ID. NO. 19 G C G C G C A G T G T A C A T C G G G G C A C T G
SEQ. ID. NO. 20 C C G A A C G C A C C C A T C A G C C A C A C T C
SEQ. ID. NO. 21 A A A A T A C C C T T A T T T C T T T T C G G A C C

SEQ. ID. NO. 18 A A C A A G A A T C A A T T C A A G T C T T T C C
SEQ. ID. NO. 19 T T T C C C A T G A G C G G G G G C T G G C C A G
SEQ. ID. NO. 20 C A C A A C C C T A C C C G C G T G A A A C T C T
SEQ. ID. NO. 21 G T C C C A T C A G A C A A T G C G G T G A A T C

SEQ. ID. NO. 18 T C C G A A C C A T C C C C A A T G A T G A G C A
SEQ. ID. NO. 19 G G G G C C A G G C C T G C C A G C C C G C G G T
SEQ. ID. NO. 20 T T G A A A A G T G G G G C T G G A A G A A G A T
SEQ. ID. NO. 21 C A G C C A T T C T G A A G T T G C T C A A G C A

SEQ. ID. NO. 18 C C A G G C C A C T G C C A T G G C A G A C A T C
SEQ. ID. NO. 19 G G A G A T G G C G C T G G A G G A C G T G A A T
SEQ. ID. NO. 20 T G C T A C C A T C C A G C A G A C C A C T G A G
SEQ. ID. NO. 21 C T A C C A G T G G A A G C G C G T G G G C A C G

FIG. 5c.

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SEQ. ID. NO. 18 A T C G A G T A T T T C C G C T G G A A C T G G G
SEQ. ID. NO. 19 A G C C G C A G G G A C A T C C T G C C G G A C T
SEQ. ID. NO. 20 G T C T T C A C T T T C G A C T C T G G A C G A C C
SEQ. ID. NO. 21 C T G A C G C A A G A C G T T C A G A G G T T C T

SEQ. ID. NO. 18 T G G G C A C A A T T G C A G C T G A T G A C G A
SEQ. ID. NO. 19 A T G A G C T C A A G C T C A T C C A C C A C G A
SEQ. ID. NO. 20 T G G A G G A A C G A G T G A A G G A G G C T G G
SEQ. ID. NO. 21 C T G A G G T G C G G A A T G A C C T G A C T G G

SEQ. ID. NO. 18 C T A T G G G C G G C C G G G G A T T G A G A A A
SEQ. ID. NO. 19 C A G C A A G T G T G A T C C A G G C C A A G C C
SEQ. ID. NO. 20 A A T T G A G A T T A C T T T C C G C C A G A G T
SEQ. ID. NO. 21 A G T T C T G T A T G G C G A G G A C A T T G A G

SEQ. ID. NO. 18 T T C C G A G A G G A A G C T G A G G A A A G G G
SEQ. ID. NO. 19 A C C A A G T A C C T A T A T G A G C T G C T C T
SEQ. ID. NO. 20 T T C T T C T C A G A T C C A G C T G T G C C C G
SEQ. ID. NO. 21 A T T T C A G A C A C C G A G A G C T T C T C C A

SEQ. ID. NO. 18 A T A T C T G C A T C G A C T T C A G T G A A C T
SEQ. ID. NO. 19 A C A A C G A C C C T A T C A A G A T C A T C C T
SEQ. ID. NO. 20 T C A A A A A C C T G A A G C G C C A G G A T G C
SEQ. ID. NO. 21 A C G A T C C C T G T A C C A G T G T C A A A A A

SEQ. ID. NO. 18 C A T C T C C C A G T A C T C T G A T G A G G A A
SEQ. ID. NO. 19 T A T G C C T G G C T G C A G C T C T G T C T C C
SEQ. ID. NO. 20 C C G A A T C A T C G T G G G A C T T T T C T A T
SEQ. ID. NO. 21 G C T G A A G G G G A A T G A T G T G C G G A T C

SEQ. ID. NO. 18 G A G A T C C A G C A T G T G G T A G A G G T G A
SEQ. ID. NO. 19 A C G C T G G T G G C T G A G G C T G C T A G G A
SEQ. ID. NO. 20 G A G A C T G A A G C C C G G A A A G T T T T T T
SEQ. ID. NO. 21 A T C C T T G G C C A G T T T G A C C A G A A T A

SEQ. ID. NO. 18 T T C A A A A T T C C A C G G C C A A A G T C A T
SEQ. ID. NO. 19 T G T G G A A C C T C A T T G T G C T T T C C T A
SEQ. ID. NO. 20 G T G A G G T G T A C A A G G A G C G T C T C T T
SEQ. ID. NO. 21 T G G C A G C A A A A G T G T T C T G T T G T G C

FIG. 5d.

15/III

SEQ. ID. NO. 18 C G T G G T T T T C T C C A G T G G C C C A G A T
SEQ. ID. NO. 19 T G G C T C C A G C T C A C C A G C C C T G T C A
SEQ. ID. NO. 20 T G G G A A G A A G T A C G T C T G G T T C C T C
SEQ. ID. NO. 21 A T A C G A G G A G A A C A T G T A T G G T A G T

SEQ. ID. NO. 18 C T T G A G C C C C T C A T C A A G G A G A T T G
SEQ. ID. NO. 19 A A C C G G C A G C G T T T C C C C A C T T T C T
SEQ. ID. NO. 20 A T T G G G T G G T A T G C T G A C A A T T G G T
SEQ. ID. NO. 21 A A A T A T C A G T G G A T C A T T C C G G G C T

SEQ. ID. NO. 18 T C C G G C G C A A T A T C A C G G G C A A G A T
SEQ. ID. NO. 19 T C C G A A C G C A C C C A T C A G C C A C A C T
SEQ. ID. NO. 20 T C A A G A T C T A C G A C C C T T C T A T C A A
SEQ. ID. NO. 21 G G T A C G A G C C T T C T T G G T G G G A G C A

SEQ. ID. NO. 18 C T G G C T G G C C A G C G A G G C C T G G G C C
SEQ. ID. NO. 19 C C A C A A C C C T A C C C G C G T G A A A C T C
SEQ. ID. NO. 20 C T G C A C A G T G G A T G A G A T G A C T G A G
SEQ. ID. NO. 21 G G T G C A C A C G G A A G C C A A C T C A T C C

SEQ. ID. NO. 18 A G C T C C T C C C T G A T C G C C A T G C C T C
SEQ. ID. NO. 19 T T T G A A A A G T G G G G C T G G A A G A A G A
SEQ. ID. NO. 20 G C G G T G G A G G G C C A C A T C A C A A C T G
SEQ. ID. NO. 21 C G C T G C C T C C G G A A G A A T C T G C T T G

SEQ. ID. NO. 18 A G T A C T T C C A C G T G G T T G G C G G C A C
SEQ. ID. NO. 19 T T G C T A C C A T C C A G C A G A C C A C T G A
SEQ. ID. NO. 20 A G A T T G T C A T G C T G A A T C C T G C C A A
SEQ. ID. NO. 21 C T G C C A T G G A G G G C T A C A T T G G C G T

SEQ. ID. NO. 18 C A T T G G A T T C G C T C T G A A G G C T G G G
SEQ. ID. NO. 19 G G T C T T C A C T T C G A C T C T G G A C G A C
SEQ. ID. NO. 20 T A C C C G C A G C A T T T C C A A C A T G A C A
SEQ. ID. NO. 21 G G A T T T C G A G C C C C T G A G C T C C A A G

SEQ. ID. NO. 18 C A G A T C C C A G G C T T C C G G G A A T T C C
SEQ. ID. NO. 19 C T G G A G G A A C G A G T G A A G G A G G C T G
SEQ. ID. NO. 20 T C C C A G G A A T T T G T G G A G A A A C T A A
SEQ. ID. NO. 21 C A G A T C A A G A C C A T C T C A G G A A A G A

FIG. 5e.

16/III

SEQ. ID. NO. 18 T G A A G A A G G T C C A T C C C A G G A A G T C
SEQ. ID. NO. 19 G A A T T G A G A T T A C T T T C C G C C A G A G
SEQ. ID. NO. 20 C C A A G C G A C T G A A A G A C A C C C T G A
SEQ. ID. NO. 21 C T C C A C A G C A G T A T G A G A G A G A G T A

SEQ. ID. NO. 18 T G T C C A C A A T G G T T T T G C C A A G G A G
SEQ. ID. NO. 19 T T T C T T C T C A G A T C C A G C T G T G C C C
SEQ. ID. NO. 20 G G A G A C A G G A G G C T T C C A G G A G G C A
SEQ. ID. NO. 21 C A A C A A C A A G C G G T C A G G C G T G G G G

SEQ. ID. NO. 18 T T T T G G G A A G A A A C A T T T A A C T G C C
SEQ. ID. NO. 19 G T C A A A A A C C T G A A G C G C C A G G A T G
SEQ. ID. NO. 20 C C G C T G G C C T A T G A T G C C A T C T G G G
SEQ. ID. NO. 21 C C C A G C A A G T T C C A C G G G T A C G C C T

SEQ. ID. NO. 18 A C C T C C A A G A A G G T G C A A A A G G A C C
SEQ. ID. NO. 19 C C C G A A T C A T C G T G G G A C T T T T T C T A
SEQ. ID. NO. 20 C C T T G G C A C T G G C C C T G A A C A A G A C
SEQ. ID. NO. 21 A C G A T G G C A T C T G G G T C A T C G C C A A

SEQ. ID. NO. 18 T T T A C C T G T G G A C A C C T T T C T G A G A
SEQ. ID. NO. 19 T G A G A C T G A A G C C C G G A A A G T T T T T
SEQ. ID. NO. 20 A T C T G G A G G A G G C G G C C G T T C T G G T
SEQ. ID. NO. 21 G A C A C T G C A G A G G G C C A T G G A G A C A

SEQ. ID. NO. 18 G G T C A C G A A G A A A G T G G C G A C A G G T
SEQ. ID. NO. 19 T G T G A G G T G T A C A A G G A G C G T C T C T
SEQ. ID. NO. 20 G T G C G C C T G G A G G A C T T C A A C T A C A
SEQ. ID. NO. 21 C T G C A T G C C A G C A G C C G G C A C C A G C

SEQ. ID. NO. 18 T T A G C A A C A G C T C G A C A G C C T T C C G
SEQ. ID. NO. 19 T T G G G A A G A A G T A C G T C T G G T T C C T
SEQ. ID. NO. 20 A C A A C C A G A C C A T T A C C G A C C A A A T
SEQ. ID. NO. 21 G G A T C C A G G A C T T C A A C T A C A C G G A

SEQ. ID. NO. 18 A C C C C T C T G T A C A G G G G A T G A G A A C
SEQ. ID. NO. 19 C A T T G G G T G G T A T G C T G A C A A T T G G
SEQ. ID. NO. 20 C T A C C G G G C A A T G A A C T C T T C G T C C
SEQ. ID. NO. 21 C C A C A C G C T G G G C A G G A T C A T C C T C

FIG. 5f.

17/III

SEQ. ID. NO. 18 A T C A G C A G T G T C G A G A C C C C T T A C A
SEQ. ID. NO. 19 T T C A A G A T C T A C G A C C C T T C T A T C A
SEQ. ID. NO. 20 T T T G A G G G T G T C T C T G G C C A T G T G G
SEQ. ID. NO. 21 A A T G C C A T G A A C G A G A C C A A C T T C T

SEQ. ID. NO. 18 T A G A T T A C A C G C A T T T A C G G A T A T C
SEQ. ID. NO. 19 A C T G C A C A G T G G A T G A G A T G A C T G A
SEQ. ID. NO. 20 T G T T T G A T G C C A G C G G C T C T C G G A T
SEQ. ID. NO. 21 T C G G G G T C A C G G G T C A A G T T G T A T T

SEQ. ID. NO. 18 C T A C A A T G T G T A C T T A G C A G T C T A C
SEQ. ID. NO. 19 G G C G G T G G A G G G C C A C A T C A C A A C T
SEQ. ID. NO. 20 G G C A T G G A C G C T T A T C G A G C A G C T T
SEQ. ID. NO. 21 C C G G A A T G G G G A G A G A A T G G G G A C C

SEQ. ID. NO. 18 T C C A T T G C C C A C G C C T T G C A A G A T A
SEQ. ID. NO. 19 G A G A T T G T C A T G C T G A A T C C T G C C A
SEQ. ID. NO. 20 C A G G G T G G C A G C T A C A A G A A G A T T G
SEQ. ID. NO. 21 A T T A A A T T T A C T C A A T T T C A A G A C A

SEQ. ID. NO. 18 T A T A T A C C T G C T T A C C T G G G A G A G G
SEQ. ID. NO. 19 A T A C C C G C A G C A T T T C C A A C A T G A C
SEQ. ID. NO. 20 G C T A C T A T G A C A G C A C C A A G G A T G A
SEQ. ID. NO. 21 G C A G G G A G G T G A A G G T G G G A G A G T A

SEQ. ID. NO. 18 G C T C T T C A C C A A T G G C T C C T G T G C A
SEQ. ID. NO. 19 A T C C C A G G A A T T T G T G G A G A A A C T A
SEQ. ID. NO. 20 T C T T T C C T G G T C C A A A A C A G A T A A A
SEQ. ID. NO. 21 C A A C G C T G T G G C C G A C A C A C T G G A G

SEQ. ID. NO. 18 G A C A T C A A G A A A G T T G A G G C G T G G C
SEQ. ID. NO. 19 A C C A A G C G A C T G A A A A G A C A C C C T G
SEQ. ID. NO. 20 T G G A T T G G A G G G T C C C C C C A G C T G
SEQ. ID. NO. 21 A T C A T C A A T G A C A C C A T C A G G T T C C

SEQ. ID. NO. 18 A G G T C C T G A A G C A C C T A C G G C A T C T
SEQ. ID. NO. 19 A G G A G A C A G G A G G C T T C C A G G A G G C
SEQ. ID. NO. 20 A C C A G A C C C T G G T C A T C A A G A C A T T
SEQ. ID. NO. 21 A A G G A T C C G A A C C A C C A A A A G A C A A

FIG. 5g.

18/III

SEQ. ID. NO. 18 A A A C T T T A C A A A C A A T A T G G G G G A G
SEQ. ID. NO. 19 A C C G C T G G C C T A T G A T G C C A T C T G G
SEQ. ID. NO. 20 C C G C T T C C T G T C A C A G A A A C T C T T T
SEQ. ID. NO. 21 G A C C A T C A T C C T G G A G C A G C T G C G G

SEQ. ID. NO. 18 C A G G T G A C C T T T G A T G A G T G T G G T G
SEQ. ID. NO. 19 G C C T T G G C A C T G G C C C T G A A C A A G A
SEQ. ID. NO. 20 A T C T C C G T C T C A G T T C T C T C C A G C C
SEQ. ID. NO. 21 A A G A T C T C C C T A C C T C T C T A C A G C A

SEQ. ID. NO. 18 A C C T G G T G G G G A A C T A T T C C A T C A T
SEQ. ID. NO. 19 C A T C T G G A G G A G G C G G C C G T T C T G G
SEQ. ID. NO. 20 T G G G C A T T G T C C T A G C T G T T G T C T G
SEQ. ID. NO. 21 T C C T C T C T G C C C T C A C C A T C C T C G G

SEQ. ID. NO. 18 C A A C T G G C A C C T C T C C C C A G A G G A T
SEQ. ID. NO. 19 T G T G C G C C T G G A G G A C T T C A A C T A C
SEQ. ID. NO. 20 T C T G T C C T T T A A C A T C T A C A A C T C A
SEQ. ID. NO. 21 G A T G A T C A T G G C C A G T G C T T T T C T C

SEQ. ID. NO. 18 G G C T C C A T C G T G T T T A A G G A A G T C G
SEQ. ID. NO. 19 A A C A A C C A G A C C A T T A C C G A C C A A A
SEQ. ID. NO. 20 C A T G T C C G T T A T A T C C A G A A C T C A C
SEQ. ID. NO. 21 T T C T T C A A C A T C A A G A A C C G G A A T C

SEQ. ID. NO. 18 G G T A T T A C A A C G T C T A T G C C A A G A A
SEQ. ID. NO. 19 T C T A C C G G G C A A T G A A C T C T T C G T C
SEQ. ID. NO. 20 A G C C C A A C C T G A A C A A C C T G A C T G C
SEQ. ID. NO. 21 A G A A G C T C A T A A A G A T G T C G A G T C C

SEQ. ID. NO. 18 G G G A G A A A G A C T C T T C A T C A A C G A G
SEQ. ID. NO. 19 C T T T G A G G G T G T C T C T G G C C A T G T G
SEQ. ID. NO. 20 T G T G G G C T G C T C A C T G G C T T T A G C T
SEQ. ID. NO. 21 A T A C A T G A A C A A C C T T A T C A T C C T T

SEQ. ID. NO. 18 G A G A A A A T C C T G T G G A G T G G G T T C T
SEQ. ID. NO. 19 G T G T T T G A T G C C A G C G G C T C T C G G A
SEQ. ID. NO. 20 G C T G T C T T C C C C C T G G G G C T C G A T G
SEQ. ID. NO. 21 G G A G G G A T G C T C T C C T A T G C T T C C A

FIG. 5h.

19/III

SEQ. ID. NO. 18 C C A G G G A G G T G C C C T T C T C C A A C T G
SEQ. ID. NO. 19 T G G C A T G G A C G C T T A T C G A G C A G C T
SEQ. ID. NO. 20 G T T A C C A C A T T G G G A G G A A C C A G T T
SEQ. ID. NO. 21 T A T T T C T C T T T G G C C T T G A T G G A T C

SEQ. ID. NO. 18 C A G C C G A G A C T G C C T G G C A G G G A C C
SEQ. ID. NO. 19 T C A G G G T G G C A G C T A C A A G A A G A T T
SEQ. ID. NO. 20 T C C T T T C G T C T G C C A G G C C C G C C T C
SEQ. ID. NO. 21 C T T T G T C T C T G A A A A G A C C T T T G A A

SEQ. ID. NO. 18 A G G A A A G G G A T C A T T G A G G G G G A G C
SEQ. ID. NO. 19 G G C T A C T A T G A C A G C A C C A A G G A T G
SEQ. ID. NO. 20 T G G C T C C T G G G C C T G G G C T T T A G T C
SEQ. ID. NO. 21 A C A C T T T G C A C C G T C A G G A C C T G G A

SEQ. ID. NO. 18 C C A C C T G C T G C T T T G A G T G T G T G G A
SEQ. ID. NO. 19 A T C T T T C C T G G T C C A A A A C A G A T A A
SEQ. ID. NO. 20 T G G G C T A C G G T T C C A T G T T C A C C A A
SEQ. ID. NO. 21 T T C T C A C C G T G G G C T A C A C G A C C G C

SEQ. ID. NO. 18 G T G T C C T G A T G G G G A G T A T A G T G A T
SEQ. ID. NO. 19 A T G G A T T G G A G G G T C C C C C C C A G C T
SEQ. ID. NO. 20 G A T T T G G T G G G T C C A C A C G G T C T T C
SEQ. ID. NO. 21 T T T T G G G G C C A T G T T T G C A A A G A C C

SEQ. ID. NO. 18 G A G A C A G A T G C C A G T G C C T G T A A C A
SEQ. ID. NO. 19 G A C C A G A C C C T G G T C A T C A A G A C A T
SEQ. ID. NO. 20 A C A A A G A A G G A A G A A A A G A A G G A G T
SEQ. ID. NO. 21 T G G A G A G T C C A C G C C A T C T T C A A A A

SEQ. ID. NO. 18 A G T G C C C A G A T G A C T T C T G G T C C A A
SEQ. ID. NO. 19 T C C G C T T C C T G T C A C A G A A A C T C T T
SEQ. ID. NO. 20 G G A G G A A G A C T C T G G A A C C C T G G A A
SEQ. ID. NO. 21 A T G T G A A A A T G A A G A A G A A G A T C A T

SEQ. ID. NO. 18 T G A G A A C C A C A C C T C C T G C A T T G C C
SEQ. ID. NO. 19 T A T C T C C G T C T C A G T T C T C T C C A G C
SEQ. ID. NO. 20 G C T G T A T G C C A C A G T G G G C C T G C T G
SEQ. ID. NO. 21 C A A G G A C C A G A A A C T G C T T G T G A T C

FIG. 5i.

20/III

SEQ. ID. NO. 18 A A G G A G A T C G A G T T T C T G T C G T G G A
SEQ. ID. NO. 19 C T G G G C A T T G T C C T A G C T G T T G T C T
SEQ. ID. NO. 20 G T G G G C A T G G A T G T C C T C A C T C T C G
SEQ. ID. NO. 21 G T G G G G G G C A T G C T G C T G A T C G A C C

SEQ. ID. NO. 18 C G G A G C C C T T T G G G A T C G C A C T C A C
SEQ. ID. NO. 19 G T C T G T C C T T T A A C A T C T A C A A C T C
SEQ. ID. NO. 20 C C A T C T G G C A G A T C G T G G A C C C T C T
SEQ. ID. NO. 21 T G T G T A T C C T G A T C T G C T G G C A G G C

SEQ. ID. NO. 18 C C T C T T T G C C G T G C T G G G C A T T T T C
SEQ. ID. NO. 19 A C A T G T C C G T T A T A T C C A G A A C T C A
SEQ. ID. NO. 20 G C A C C G G A C C A T T G A G A C A T T T G C C
SEQ. ID. NO. 21 T G T G G A C C C C C T G C G A A G G A C A G T G

SEQ. ID. NO. 18 C T G A C A G C C T T T G T G C T G G G T G T G T
SEQ. ID. NO. 19 C A G C C C A A C C T G A A C A A C C T G A C T G
SEQ. ID. NO. 20 A A G G A G G A A C C T A A G G A A G A T A T T G
SEQ. ID. NO. 21 G A G A A G T A C A G C A T G G A G C C G G A C C

SEQ. ID. NO. 18 T T A T C A A G T T C C G C A A C A C A C C C A T
SEQ. ID. NO. 19 C T G T G G G C T G C T C A C T G G C T T T A G C
SEQ. ID. NO. 20 A C G T C T C T A T T C T G C C C C A G C T G G A
SEQ. ID. NO. 21 C A G C A G G A C G G G A T A T C T C C A T C C G

SEQ. ID. NO. 18 T G T C A A G G C C A C C A A C C G A G A G C T C
SEQ. ID. NO. 19 T G C T G T C T T C C C C C T G G G G C T C G A T
SEQ. ID. NO. 20 G C A T T G C A G C T C C A G G A A G A T G A A T
SEQ. ID. NO. 21 C C C T C T C C T G G A G C A C T G T G A G A A C

SEQ. ID. NO. 18 T C C T A C C T C C T C C T C T T C T C C C T G C
SEQ. ID. NO. 19 G G T T A C C A C A T T G G G A G G A A C C A G T
SEQ. ID. NO. 20 A C A T G G C T T G G C A T T T T C T A T G G T T
SEQ. ID. NO. 21 A C C C A T A T G A C C A T C T G G C T T G G C A

SEQ. ID. NO. 18 T C T G C T G C T T C T C C A G C T C C C T G T T
SEQ. ID. NO. 19 T T C C T T T C G T C T G C C A G G C C C G C C T
SEQ. ID. NO. 20 A C A A G G G G C T G C T G C T G C T G G G
SEQ. ID. NO. 21 T C G T C T A T G C C T A C A A G G G A C T T C T

FIG. 5j.

SUBSTITUTE SHEET (RULE 26)

21/III

SEQ. ID. NO. 18 C T T C A T C G G G G A G C C C C A G G A C T G G
SEQ. ID. NO. 19 C T G G C T C C T G G G C C T G G G C T T T A G T
SEQ. ID. NO. 20 A A T C T T C C T T G C T T A T G A G A C C A A G
SEQ. ID. NO. 21 C A T G T T G T T C G G T T G T T T C T T A G C T

SEQ. ID. NO. 18 A C G T G C C G C C T G C G C C A G C C G G C C T
SEQ. ID. NO. 19 C T G G G C T A C G G T T C C A T G T T C A C C A
SEQ. ID. NO. 20 A G T G T G T C C A C T G A G A A G A T C A A T G
SEQ. ID. NO. 21 T G G G A G A C C C G C A A C G T C A G C A T C C

SEQ. ID. NO. 18 T T G G C A T C A G C T T C G T G C T C T G C A T
SEQ. ID. NO. 19 A G A T T T G G T G G G T C C A C A C G G T C T T
SEQ. ID. NO. 20 A T C A C C G G G C T G T G G G C A T G G C T A T
SEQ. ID. NO. 21 C C G C A C T C A A C G A C A G C A A G T A C A T

SEQ. ID. NO. 18 C T C A T G C A T C C T G G T G A A A A C C A A C
SEQ. ID. NO. 19 C A C A A A G A A G G A A G A A A A G A A G G A G
SEQ. ID. NO. 20 C T A C A A T G T G G C A G T C C T G T G C C T C
SEQ. ID. NO. 21 C G G G A T G A G T G T C T A C A A C G T G G G G

SEQ. ID. NO. 18 C G T G T C C T C C T G G T G T T T G A G G C C A
SEQ. ID. NO. 19 T G G A G G A A G A C T C T G G A A C C C T G G A
SEQ. ID. NO. 20 A T C A C T G C T C C T G T C A C C A T G A T T C
SEQ. ID. NO. 21 A T C A T G T G C A T C A T C G G G G C C G C T G

SEQ. ID. NO. 18 A G A T C C C C A C C A G C T T C C A C C G C A A
SEQ. ID. NO. 19 A G C T G T A T G C C A C A G T G G G C C T G C T
SEQ. ID. NO. 20 T G T C C A G C C A G C A G G A T G C A G C C T T
SEQ. ID. NO. 21 T C T C C T T C C T G A C C C G G G A C C A G C C

SEQ. ID. NO. 18 G T G G T G G G G G C T C A A C C T G C A G T T C
SEQ. ID. NO. 19 G G T G G G C A T G G A T G T C C T C A C T C T C
SEQ. ID. NO. 20 T G C C T T T G C C T C T C T T G C C A T A G T T
SEQ. ID. NO. 21 C A A T G T G C A G T T C T G C A T C G T G G C T

SEQ. ID. NO. 18 C T G C T G G T T T T C C T C T G C A C C T T C A
SEQ. ID. NO. 19 G C C A T C T G G C A G A T C G T G G A C C C T C
SEQ. ID. NO. 20 T T C T C C T C C T A T A T C A C T C T T G T T G
SEQ. ID. NO. 21 C T G G T C A T C A T C T T C T G C A G C A C C A

FIG. 5k.

22/III

SEQ. ID. NO. 18 T G C A G A T T G T C A T C T G T G T G A T C T G
SEQ. ID. NO. 19 T G C A C C G G A C C A T T G A G A C A T T T G C
SEQ. ID. NO. 20 T G C T C T T T G T G C C C A A G A T G C G C A G
SEQ. ID. NO. 21 T C A C C C T C T G C C T G G T A T T C G T G C C

SEQ. ID. NO. 18 G C T C T A C A C C G C G C C C C C C T C A A G C
SEQ. ID. NO. 19 C A A G G A G G A A C C T A A G G A A G A T A T T
SEQ. ID. NO. 20 G C T G A T C A C C C G A G G G G A A T G G C A G
SEQ. ID. NO. 21 G A A G C T C A T C A C C C T G A G A A C A A A C

SEQ. ID. NO. 18 T A C C G C A A C C A G G A G C T G G A G G A T G
SEQ. ID. NO. 19 G A C G T C T C T A T T C T G C C C C A G C T G G
SEQ. ID. NO. 20 T C G G A G G C G C A G G A C A C C A T G A A G A
SEQ. ID. NO. 21 C C A G A T G C A G C A A C G C A G A A C A G G C

SEQ. ID. NO. 18 A G A T C A T C T T C A T C A C G T G C C A C G A
SEQ. ID. NO. 19 A G C A T T G C A G C T C C A G G A A G A T G A A
SEQ. ID. NO. 20 C A G G G T C A T C G A C C A A C A A C A A C G A
SEQ. ID. NO. 21 G A T T C C A G T T C A C T C A G A A T C A G A A

SEQ. ID. NO. 18 G G G C T C C C T C A T G G C C C T G G G C T T C
SEQ. ID. NO. 19 T A C A T G G C T T G G C A T T T T C T A T G G T
SEQ. ID. NO. 20 G G A G G A G A A G T C C C G G C T G T T G G A G
SEQ. ID. NO. 21 G A A A G A A G A T T C T A A A A C G T C C A C C

SEQ. ID. NO. 18 C T G A T C G G C T A C A C C T G C C T G C T G G
SEQ. ID. NO. 19 T A C A A G G G G C T G C T G C T G C T G C T G G
SEQ. ID. NO. 20 A A G G A G A A C C G T G A A C T G G A A A A G A
SEQ. ID. NO. 21 T C G G T C A C C A G T G T G A A C C A A G C C A

SEQ. ID. NO. 18 C T G C C A T C T G C T T C T T C T T T G C C T T
SEQ. ID. NO. 19 G A A T C T T C C T T G C T T A T G A G A C C A A
SEQ. ID. NO. 20 T C A T T G C T G A G A A A G A G G A G C G T G T
SEQ. ID. NO. 21 G C A C A T C C C G C C T G G A G G G C C T A C A

SEQ. ID. NO. 18 C A A G T C C C G G A A G C T G C C G G A G A A C
SEQ. ID. NO. 19 G A G T G T G T C C A C T G A G A A G A T C A A T
SEQ. ID. NO. 20 C T C T G A A C T G C G C C A T C A A C T C C A G
SEQ. ID. NO. 21 G T C A G A A A A C C A T C G C C T G C G A A T G

FIG. 5L.

SUBSTITUTE SHEET (RULE 26)

23/III

SEQ. ID. NO. 18 T T C A A T G A A G C C A A G T T C A T C A C C T
SEQ. ID. NO. 19 G A T C A C C G G G C T G T G G G C A T G G C T A
SEQ. ID. NO. 20 T C T C G G C A G C A G C T C C G C T C C C G G C
SEQ. ID. NO. 21 A A G A T C A C A G A G C T G G A T A A A G A C T

SEQ. ID. NO. 18 T C A G C A T G C T C A T C T T C T T C A T C G T
SEQ. ID. NO. 19 T C T A C A A T G T G G C A G T C C T G T G C C T
SEQ. ID. NO. 20 G C C A C C C A C C G A C A C C C C C A G A A C C
SEQ. ID. NO. 21 T G G A A G A G G T C A C C A T G C A G C T G C A

SEQ. ID. NO. 18 C T G G A T C T C C T T C A T T C C A G C C T A T
SEQ. ID. NO. 19 C A T C A C T G C T C C T G T C A C C A T G A T T
SEQ. ID. NO. 20 C T C T G G G G G C C T G C C C A G G G G A C C C
SEQ. ID. NO. 21 G G A C A C A C C A G A A A A G A C C A C C T A C

SEQ. ID. NO. 18 G C C A G C A C C T A T G G C A A G T T T G T C T
SEQ. ID. NO. 19 C T G T C C A G C C A G C A G G A T G C A G C C T
SEQ. ID. NO. 20 C C T G A G C C C C C G A C C G G C T T A G C T
SEQ. ID. NO. 21 A T T A A A C A G A A C C A C T A C C A A G A G C

SEQ. ID. NO. 18 C T G C C G T A G A G G T G A T T G C C A T C C T
SEQ. ID. NO. 19 T T G C C T T T G C C T C T C T T G C C A T A G T
SEQ. ID. NO. 20 G T G A T G G G A G T C G A G T G C A T T T G C T
SEQ. ID. NO. 21 T C A A T G A C A T C C T C A A C C T G G G A A A

SEQ. ID. NO. 18 G G C A G C C A G C T T T G G C T T G C T G G C G
SEQ. ID. NO. 19 T T T C T C C T C C T A T A T C A C T C T T G T T
SEQ. ID. NO. 20 T T A T A A G T G A G G G T A G G G T G A G G G A
SEQ. ID. NO. 21 C T T C A C T G A G A G C A C A G A T G G A G G A

SEQ. ID. NO. 18 T G C A T C T T C T T C A A C A A G A T C T A C A
SEQ. ID. NO. 19 G T G C T C T T T G T G C C C A A G A T G C G C A
SEQ. ID. NO. 20 G G A C A G G C C A G T A G G G G G A G G G A A A
SEQ. ID. NO. 21 A A G G C C A T T T T A A A A A A T C A C C T C G

SEQ. ID. NO. 18 T C A T T C T C T T C A A G C C A T C C C G C A A
SEQ. ID. NO. 19 G G C T G A T C A C C C G A G G G G A A T G G C A
SEQ. ID. NO. 20 G G G A G A G G G G A A G G G C A G G G G A C T C
SEQ. ID. NO. 21 A T C A A A A T C C C C A G C T A C A G T G G A A

FIG. 5m.

24/III

SEQ. ID. NO. 18 C A C C A T C G A G G A G G T G C G T T G C A G C
SEQ. ID. NO. 19 G T C G G A G G C G C A G G A C A C C A T G A A G
SEQ. ID. NO. 20 A G G A A G C A G G G G G T C C C C A T C C C C A
SEQ. ID. NO. 21 C A C A A C A G A G C C C T C T C G A A C A T G C

SEQ. ID. NO. 18 A C C G C A G C T C A C G C T T T C A A G G T G G
SEQ. ID. NO. 19 A C A G G G T C A T C G A C C A A C A A C A A C G
SEQ. ID. NO. 20 G C T G G G A A G A A C A T G C T A T C C A A T C
SEQ. ID. NO. 21 A A A G A T C C T A T A G A A G A T A T A A A C T

SEQ. ID. NO. 18 C T G C C C G G G C C A C G C T G C G C C G C A G
SEQ. ID. NO. 19 A G G A G G A G A A G T C C C G G C T G T T G G A
SEQ. ID. NO. 20 T C A T C T C T T G T A A A T A C A T G T C C C C
SEQ. ID. NO. 21 C T C C A G A A C A C A T C C A G C G T C G G C T

SEQ. ID. NO. 18 C A A C G T C T C C C G C A A G C G G T C C A G C
SEQ. ID. NO. 19 G A A G G A G A A C C G T G A A C T G G A A A A G
SEQ. ID. NO. 20 C T G T G A G T T C T G G G C T G A T T T G G G T
SEQ. ID. NO. 21 G T C C C T C C A G C T C C C C A T C C T C C A C

SEQ. ID. NO. 18 A G C C T T G G A G G C T C C A C G G G A T C C A
SEQ. ID. NO. 19 A T C A T T G C T G A G A A A G A G G A G C G T G
SEQ. ID. NO. 20 C T C T C A T A C C T C T G G G A A A C A G A C C
SEQ. ID. NO. 21 C A C G C C T A C C T C C C A T C C A T C G G A G

SEQ. ID. NO. 18 C C C C C T C C T C C T C C A T C A G C A G C A A
SEQ. ID. NO. 19 T C T C T G A A C T G C G C C A T C A G C T C C A
SEQ. ID. NO. 20 T T T T T C T C T C T T A C T G C T T C A T G T A
SEQ. ID. NO. 21 G C G T G G A C G C C A G C T G T G T C A G C C C

SEQ. ID. NO. 18 G A G C A A C A G C G A A G A C C C A T T C C C A
SEQ. ID. NO. 19 G T C T C G G C A G C A G C T C C G C T C C C G G
SEQ. ID. NO. 20 A T T T T G T A T C A C C T C T T C A C A A T T T
SEQ. ID. NO. 21 C T G C G T C A G C C C C A C C G C C A G C C C C

SEQ. ID. NO. 18 C A G C C C G A G A G G C A G A A G C A G C A G C
SEQ. ID. NO. 19 C G C C A C C C A C C G A C A C C C C C A G A A C
SEQ. ID. NO. 20 A G T T C G T A C C T G G C T T G A A G C T G C T
SEQ. ID. NO. 21 C G C C A C A G A C A T G T G C C A C C C T C C T

FIG. 5n.

25/III

SEQ. ID. NO. 18 A G C C G C T G G C C C T A A C C C A G C A A G A
SEQ. ID. NO. 19 C C T C T G G G G G C C T G C C C A G G G G A C C
SEQ. ID. NO. 20 C A C T G C T C A C A C G C T G C C T C C T C A G
SEQ. ID. NO. 21 T C C G A G T C A T G G T C T C G G G C C T G T A

SEQ. ID. NO. 18 G C A G C A G C A G C A G C C C C T G A C C C T C
SEQ. ID. NO. 19 C C C T G A G C C C C C C G A C C G G C T T A G C
SEQ. ID. NO. 20 C A G C C T C A C T G C A T C T T T C T C T T C C
SEQ. ID. NO. 21 A G G G T G G G A G G C C T G G G C C C G G G G C

SEQ. ID. NO. 18 C C A C A G C A G C A A C G A T C T C A G C A G C
SEQ. ID. NO. 19 T G T G A T G G G A G T C G A G T G C A T T T G C
SEQ. ID. NO. 20 C A T G C A A C A C C C T C T T C T A G T T A C C
SEQ. ID. NO. 21 C T C C C C C G T G A C A G A A C C A C A C T G G

SEQ. ID. NO. 18 A G C C C A G A T G C A A G C A G A A G G T C A T
SEQ. ID. NO. 19 T T T A T A A G T G A G G G T A G G G T G A G G G
SEQ. ID. NO. 20 A C G G C A A C C C C T
SEQ. ID. NO. 21 G C A G A G G G G T C T G C T G C A G A A A C A C

SEQ. ID. NO. 18 C T T T G G C A G C G G C A C G G T C A C C T T C
SEQ. ID. NO. 19 A G G A C A G G C C A G T A G G G G G A G G G A A
SEQ. ID. NO. 20
SEQ. ID. NO. 21 T G T C G G C T C T G G C T G C G G A G A A G C T

SEQ. ID. NO. 18 T C A C T G A G C T T T G A T G A G C C T C A G A
SEQ. ID. NO. 19 A G G G A G A G G G G A A G G G C A G G G G A C T
SEQ. ID. NO. 20
SEQ. ID. NO. 21 G G G C A C C A T G G C T G G C C T C T C A G G A

SEQ. ID. NO. 18 A G A A C G C C A T G G C C C A C G G G A A T T C
SEQ. ID. NO. 19 C A G G A A G C A G G G G G T C C C C A T C C C C
SEQ. ID. NO. 20
SEQ. ID. NO. 21 C C A C T C G G A T G G C A C T C A G G T G G A C

SEQ. ID. NO. 18 T A C G C A C C A G A A C T C C C T G G A G G C C
SEQ. ID. NO. 19 A G C T G G G A A G A A C A T G C T A T C C A A T
SEQ. ID. NO. 20
SEQ. ID. NO. 21 A G G A C G G G G C A G G G G G A G A C T T G G C

FIG. 50.

26/III

SEQ. ID. NO. 18 C A G A A A A G C A G C G A T A C G C T G A C C C
SEQ. ID. NO. 19 C T C A T C T C T T G T A A A T A C A T G T C C C
SEQ. ID. NO. 20
SEQ. ID. NO. 21 A C C T G A C C T C G A G C C T T A T T T G T G A

SEQ. ID. NO. 18 G A C A C C A G C C A T T A C T C C C G C T G C A
SEQ. ID. NO. 19 C C T G T G A G T T C T G G G C T G A T T T G G G
SEQ. ID. NO. 20
SEQ. ID. NO. 21 A G T C C T T A T T T C T T C A C A A A G A A G A

SEQ. ID. NO. 18 G T G C G G G G A A A C G G A C T T A G A T C T G
SEQ. ID. NO. 19 T C T C T C A T A C C T C T G G G A A A C A G A C
SEQ. ID. NO. 20
SEQ. ID. NO. 21 G G A A C G G A A A T G G G A C G T C T T C C T T

SEQ. ID. NO. 18 A C C G T C C A G G A A A C A G G T C T G C A A G
SEQ. ID. NO. 19 C T T T T T C T C T C T T A C T G C T T C A T G T
SEQ. ID. NO. 20
SEQ. ID. NO. 21 A A C A T C T G C A A A C A A G G A G G C G C T G

SEQ. ID. NO. 18 G A C C T G T G G G T G G A G A C C A G C G G C C
SEQ. ID. NO. 19 A A T T T T G T A T C A C C T C T T C A C A A T T
SEQ. ID. NO. 20
SEQ. ID. NO. 21 G G A T A T C A A A C T T G C A A A A A A A A A A

SEQ. ID. NO. 18 A G A G G T G G A G G A C C C T G A A G A G T T G
SEQ. ID. NO. 19 T A G T T C G T A C C T G G C T T G A A G C T G C
SEQ. ID. NO. 20
SEQ. ID. NO. 21 A A A A A A A A A A A A

SEQ. ID. NO. 18 T C C C C A G C A C T T G T A G T G T C C A G T T
SEQ. ID. NO. 19 T C A C T G C T C A C A C G C T G C C T C C T C A
SEQ. ID. NO. 20
SEQ. ID. NO. 21

SEQ. ID. NO. 18 C A C A G A G C T T T G T C A T C A G T G G T G G
SEQ. ID. NO. 19 G C A G C C T C A C T G C A T C T T T C T C T T C
SEQ. ID. NO. 20
SEQ. ID. NO. 21

FIG. 5p.

27/III

SEQ. ID. NO. 18 A G G C A G C A C T G T T A C A G A A A A C G T A
SEQ. ID. NO. 19 C C A T G C A A C A C C C T C T T C T A G T T A C
SEQ. ID. NO. 20
SEQ. ID. NO. 21

SEQ. ID. NO. 18 G T G A A T T C A
SEQ. ID. NO. 19 C A C G G C A A C C C C T G C A G C T C C T C T G
SEQ. ID. NO. 20
SEQ. ID. NO. 21

SEQ. ID. NO. 18
SEQ. ID. NO. 19 C C T T T G T G C T C T G T T C C T G T C C A G C
SEQ. ID. NO. 20
SEQ. ID. NO. 21

SEQ. ID. NO. 18
SEQ. ID. NO. 19 A G G G G T C T C C C A A C A A G T G C T C T T T
SEQ. ID. NO. 20
SEQ. ID. NO. 21

SEQ. ID. NO. 18
SEQ. ID. NO. 19 C C A C C C C A A A G G G G C C T C T C C T T T T
SEQ. ID. NO. 20
SEQ. ID. NO. 21

SEQ. ID. NO. 18
SEQ. ID. NO. 19 C T C C A C T G T C A T A A T C T C T T T C C A T
SEQ. ID. NO. 20
SEQ. ID. NO. 21

SEQ. ID. NO. 18
SEQ. ID. NO. 19 C T T A C T T G C C C T T C T A T A C T T T T C T C
SEQ. ID. NO. 20
SEQ. ID. NO. 21

SEQ. ID. NO. 18
SEQ. ID. NO. 19 A C A T G T G G C T C C C C C T G A A T T T T G C
SEQ. ID. NO. 20
SEQ. ID. NO. 21

FIG. 5q.

28/III

SEQ. ID. NO. 18
SEQ. ID. NO. 19 T T C C T T T G G G G A G C T C A T T C T T T C G
SEQ. ID. NO. 20
SEQ. ID. NO. 21

SEQ. ID. NO. 18
SEQ. ID. NO. 19 C C A A G G T C A C A T G C T C C C T T G C C T C
SEQ. ID. NO. 20
SEQ. ID. NO. 21

SEQ. ID. NO. 18
SEQ. ID. NO. 19 T G G C T C C G T G C A
SEQ. ID. NO. 20
SEQ. ID. NO. 21

FIG. 5r.

29/III

SEQ. ID. NO. 22 A T G C T G C T G C T G C T G C T G G T G C C T C T C T T C
SEQ. ID. NO. 23 A T G G G C C C G G G G G G A C C C T G T A C C C C A G T G

SEQ. ID. NO. 22 C T C C G C C C C C T G G G C G C T G G C G G G G C G C A G
SEQ. ID. NO. 23 G G G T G G C C G C T G C C T C T T C T G C T G G T G A T G

SEQ. ID. NO. 22 A C C C C C A A C G C C A C C T C G G A A G G T T G C C A G
SEQ. ID. NO. 23 G C G G C T G G G G T G G C T C C G G T G T G G G C C T C T

SEQ. ID. NO. 22 A T T A T A C A T C C G C C C T G G G A A G G T G G C A T C
SEQ. ID. NO. 23 C A C T C C C C T C A T C T C C C G C G G C C T C A C C C G

SEQ. ID. NO. 22 A G G T A C C G T G G C T T G A C T C G C G A C C A G G T G
SEQ. ID. NO. 23 A G G G T C C C C C C G C A C C C C T C C T C A G A A C G G

SEQ. ID. NO. 22 A A G G C C A T C A A C T T C C T G C C T G T G G A C T A T
SEQ. ID. NO. 23 C G T G C A G T A T A C A T C G G G G C G C T G T T T C C C

SEQ. ID. NO. 22 G A G A T C G A A T A T G T G T G C C G A G G G G A G C G C
SEQ. ID. NO. 23 A T G A G C G G G G G C T G G C C G G G G G C C A G G C C

SEQ. ID. NO. 22 G A G G T G G T G G G G C C C A A G G T G C G C A A A T G C
SEQ. ID. NO. 23 T G C C A G C C C G C G G T G G A G A T G G C G C T G G A G

SEQ. ID. NO. 22 C T G G C C A A C G G C T C C T G G A C G G A T A T G G A C
SEQ. ID. NO. 23 G A C G T T A A C A G C C G C A G A G A C A T C C T G C C G

SEQ. ID. NO. 22 A C A C C C A G C C G C T G T G T C C G A A T C T G C T C C
SEQ. ID. NO. 23 G A C T A C G A G C T C A A G C T T A T C C A C C A C G A C

SEQ. ID. NO. 22 A A G T C T T A T T T G A C C C T G G A A A A T G G G A A G
SEQ. ID. NO. 23 A G C A A G T G T G A C C C A G G G C A A G C C A C C A A G

SEQ. ID. NO. 22 G T T T T C C T G A C G G G T G G G G A C C T C C C A G C T
SEQ. ID. NO. 23 T A C T T G T A C G A A C T A C T C T A C A A T G A C C C C

FIG. 6a.

30/III

SEQ. ID. NO. 22 C T G G A T G G A G C C C G G G T G G A G T T C C G A T G T
SEQ. ID. NO. 23 A T C A A G A T C A T T C T C A T G C C T G G C T G T A G T

SEQ. ID. NO. 22 G A C C C C G A C T T C C A T C T G G T G G G C A G C T C C
SEQ. ID. NO. 23 T C T G T C T C C A C A C T T G T A G C T G A G G C T G C C

SEQ. ID. NO. 22 C G G A G C G T C T G T A G T C A G G G C C A G T G G A G C
SEQ. ID. NO. 23 C G G A T G T G G A A C C T T A T T G T G C T C T C A T A T

SEQ. ID. NO. 22 A C C C C C A A G C C C C A C T G C C A G G T G A A T C G A
SEQ. ID. NO. 23 G G C T C C A G T T C A C C A G C C T T G T C A A A C C G A

SEQ. ID. NO. 22 A C G C C A C A C T C A G A A C G G C G T G C A G T A T A C
SEQ. ID. NO. 23 C A G C G G T T T C C C A C G T T C T T C C G G A C G C A T

SEQ. ID. NO. 22 A T C G G G G C G C T G T T T C C C A T G A G C G G G G G C
SEQ. ID. NO. 23 C C A T C C G C C A C A C T C C A C A A T C C C A C C C G G

SEQ. ID. NO. 22 T G G C C G G G G G G C C A G G C C T G C C A G C C C G C G
SEQ. ID. NO. 23 G T G A A A C T C T T C G A A A A G T G G G G C T G G A A G

SEQ. ID. NO. 22 G T G G A G A T G G C G C T G G A G G A C G T T A A C A G C
SEQ. ID. NO. 23 A A G A T C G C T A C C A T C C A A C A G A C C A C C G A G

SEQ. ID. NO. 22 C G C A G A G A C A T C C T G C C G G A C T A C G A G C T C
SEQ. ID. NO. 23 G T C T T C A C C T C A A C G C T G G A T G A C C T G G A G

SEQ. ID. NO. 22 A A G C T T A T C C A C C A C G A C A G C A A G T G T G A C
SEQ. ID. NO. 23 G A G C G A G T G A A A G A G G C T G G G A T C G A G A T C

SEQ. ID. NO. 22 C C A G G G C A A G C C A C C A A G T A C T T G T A C G A A
SEQ. ID. NO. 23 A C T T T C C G A C A G A G T T T C T T C T C G G A T C C A

SEQ. ID. NO. 22 C T A C T C T A C A A T G A C C C C A T C A A G A T C A T T
SEQ. ID. NO. 23 G C T G T G C C T G T T A A A A A C C T G A A G C G T C A A

SEQ. ID. NO. 22 C T C A T G C C T G G C T G T A G T T C T G T C T C C A C A
SEQ. ID. NO. 23 G A T G C T C G A A T C A T C G T G G G A C T T T T C T A T

FIG. 6b.

SUBSTITUTE SHEET (RULE 26)

31/III

SEQ. ID. NO. 22 C T T G T A G C T G A G G C T G C C C G G A T G T G G A A C
SEQ. ID. NO. 23 G A G A C G G A A G C C C G G A A A G T T T T T T G T G A G

SEQ. ID. NO. 22 C T T A T T G T G C T C T C A T A T G G C T C C A G T T C A
SEQ. ID. NO. 23 G T C T A T A A G G A A A G G C T C T T T G G G A A G A A G

SEQ. ID. NO. 22 C C A G C C T T G T C A A A C C G A C A G C G G T T T C C C
SEQ. ID. NO. 23 T A C G T C T G G T T C C T C A T C G G G T G G T A T G C T

SEQ. ID. NO. 22 A C G T T C T T C C G G A C G C A T C C A T C C G C C A C A
SEQ. ID. NO. 23 G A C A A C T G G T T C A A G A C C T A T G A C C C G T C A

SEQ. ID. NO. 22 C T C C A C A A T C C C A C C C G G G T G A A A C T C T T C
SEQ. ID. NO. 23 A T C A A T T G T A C A G T G G A A G A A A T G A C C G A G

SEQ. ID. NO. 22 G A A A A G T G G G G C T G G A A G A A G A T C G C T A C C
SEQ. ID. NO. 23 G C G G T G G A G G G C C A C A T C A C C A C G G A G A T T

SEQ. ID. NO. 22 A T C C A A C A G A C C A C C G A G G T C T T C A C C T C A
SEQ. ID. NO. 23 G T C A T G C T G A A C C C T G C C A A C A C C C G A A G C

SEQ. ID. NO. 22 A C G C T G G A T G A C C T G G A G G A G C G A G T G A A A
SEQ. ID. NO. 23 A T T T C C A A C A T G A C G T C A C A G G A A T T T G T G

SEQ. ID. NO. 22 G A G G C T G G G A T C G A G A T C A C T T T C C G A C A G
SEQ. ID. NO. 23 G A G A A A C T A A C C A A G C G G C T G A A A A G A C A C

SEQ. ID. NO. 22 A G T T T C T T C T C G G A T C C A G C T G T G C C T G T T
SEQ. ID. NO. 23 C C C G A G G A G A C T G G A G G C T T C C A G G A G G C A

SEQ. ID. NO. 22 A A A A A C C T G A A G C G T C A A G A T G C T C G A A T C
SEQ. ID. NO. 23 C C A C T G G C C T A T G A T G C T A T C T G G G C C T T G

SEQ. ID. NO. 22 A T C G T G G G A C T T T T T C T A T G A G A C G G A A G C C
SEQ. ID. NO. 23 G C T T T G G C C T T G A A C A A G A C G T C T G G A G G A

SEQ. ID. NO. 22 C G G A A A G T T T T T T G T G A G G T C T A T A A G G A A
SEQ. ID. NO. 23 G G T G G T C G T T C C G G C G T G C G C C T G G A G G A C

FIG. 6c.

32/III

SEQ. ID. NO. 22 A G G C T C T T T G G G A A G A A G T A C G T C T G G T T C
SEQ. ID. NO. 23 T T T A A C T A C A A C A A C C A G A C C A T T A C A G A C

SEQ. ID. NO. 22 C T C A T C G G G T G G T A T G C T G A C A A C T G G T T C
SEQ. ID. NO. 23 C A G A T C T A C C G G G C C A T G A A C T C C T C C T C C

SEQ. ID. NO. 22 A A G A C C T A T G A C C C G T C A A T C A A T T G T A C A
SEQ. ID. NO. 23 T T T G A G G G C G T T T C T G G C C A T G T G G T C T T T

SEQ. ID. NO. 22 G T G G A A G A A A T G A C C G A G G C G G T G G A G G G C
SEQ. ID. NO. 23 G A T G C C A G C G G C T C C C G G A T G G C A T G G A C A

SEQ. ID. NO. 22 C A C A T C A C C A C G G A G A T T G T C A T G C T G A A C
SEQ. ID. NO. 23 C T T A T C G A G C A G C T A C A G G G C G G C A G C T A C

SEQ. ID. NO. 22 C C T G C C A A C A C C C G A A G C A T T T C C A A C A T G
SEQ. ID. NO. 23 A A G A A G A T C G G C T A C T A C G A C A G C A C C A A G

SEQ. ID. NO. 22 A C G T C A C A G G A A T T T G T G G A G A A A C T A A C C
SEQ. ID. NO. 23 G A T G A T C T T T C C T G G T C C A A A A C G G A C A A G

SEQ. ID. NO. 22 A A G C G G C T G A A A A G A C A C C C C G A G G A G A C T
SEQ. ID. NO. 23 T G G A T T G G A G G G T C T C C C C C A G C T G A C C A G

SEQ. ID. NO. 22 G G A G G C T T C C A G G A G G C A C C A C T G G C C T A T
SEQ. ID. NO. 23 A C C T T G G T C A T C A A G A C A T T C C G T T T C C T G

SEQ. ID. NO. 22 G A T G C T A T C T G G G C C T T G G C T T T G G C C T T G
SEQ. ID. NO. 23 T C T C A G A A A C T C T T T A T C T C C G T C T C A G T T

SEQ. ID. NO. 22 A A C A A G A C G T C T G G A G G A G G T G G T C G T T C C
SEQ. ID. NO. 23 C T C T C C A G C C T G G G C A T T G T T C T T G C T G T T

SEQ. ID. NO. 22 G G C G T G C G C C T G G A G G A C T T T A A C T A C A A C
SEQ. ID. NO. 23 G T C T G T C T G T C C T T T A A C A T C T A C A A C T C C

SEQ. ID. NO. 22 A A C C A G A C C A T T A C A G A C C A G A T C T A C C G G
SEQ. ID. NO. 23 C A C G T T C G T T A T A T C C A G A A C T C C C A G C C C

FIG. 6d.

33/III

SEQ. ID. NO. 22 GCCATGAACTCCTCCTCCTTTGAGGGCGTT
SEQ. ID. NO. 23 AACCTGAACAATCTGACTGCTGTGGGCTGC

SEQ. ID. NO. 22 TCTGGCCATGTGGTCTTTGATGCCAGCGGC
SEQ. ID. NO. 23 TCACTGGCACTGGCTGCTGTCTTCCCTCTC

SEQ. ID. NO. 22 TCCCGGATGGCATGGACACTTATCGAGCAG
SEQ. ID. NO. 23 GGGCTGGATGGTTACCAACATAGGGAGAAC

SEQ. ID. NO. 22 CTACAGGGCGGGCAGCTACAAGAAAGATCGGC
SEQ. ID. NO. 23 CAGTTCCCGTTTGTCTGCCAGGCCCGCCTT

SEQ. ID. NO. 22 TACTACGACAGCACCAAGGATGATCTTTCC
SEQ. ID. NO. 23 TGGCTCTTGGGCTTGGGCTTTAGTCTGGGC

SEQ. ID. NO. 22 TGGTCCAAAACGGACAAAGTGGATTGGAGGG
SEQ. ID. NO. 23 TATGGCTCTATGTTCAACCAAGATCTGGTGG

SEQ. ID. NO. 22 TCTCCCCCAGCTGACCAGACCTTGGGTCATC
SEQ. ID. NO. 23 GTCCACACAGTCTTCAACGAAGAAGGAGGAG

SEQ. ID. NO. 22 AAGACATTCCGTTTCTCTGTCTCAGAAACTC
SEQ. ID. NO. 23 AAGAAAGGAGTGGAGGAAGACCCTAGAGCCC

SEQ. ID. NO. 22 TTTATCTCCGTCTCAGTTCTCTCCAGCCTG
SEQ. ID. NO. 23 TGGAAACTCTATGCCACTGTGGGCCTGCTG

SEQ. ID. NO. 22 GGCATTGTTCTTGGCTGTTGTCTGTCTGTCC
SEQ. ID. NO. 23 GTGGGCAATGGATGTCCTGACTCTTGGCCATC

SEQ. ID. NO. 22 TTTAACATCTACAACCTCCCAAGTTTCGTTAT
SEQ. ID. NO. 23 TGGCAGATTGTGGACCCCTTGCAACCGAAC

SEQ. ID. NO. 22 ATCCAGAACTCCCAAGCCCAACCTGAACAAT
SEQ. ID. NO. 23 ATTGAGACTTTTGCCAAGGAGGAACCAAG

SEQ. ID. NO. 22 CTGACTGCTGTGGGCTGCTCACTGGCACTG
SEQ. ID. NO. 23 GAAGACATCGATGTCTCCATTCTGCCCCAG

FIG. 6e.

34/III

SEQ. ID. NO. 22 G C T G C T G T C T T C C C T C T C G G G C T G G A T G G T
SEQ. ID. NO. 23 T T G G A G C A C T G C A G C T C C A A G A A G A T G A A T

SEQ. ID. NO. 22 T A C C A C A T A G G G A G A A G C C A G T T C C C G T T T
SEQ. ID. NO. 23 A C G T G G C T T G G C A T T T T C T A T G G T T A C A A G

SEQ. ID. NO. 22 G T C T G C C A G G C C C G C C T T T G G C T C T T G G G C
SEQ. ID. NO. 23 G G G C T G C T G C T G C T G C T G G G A A T C T T T C T T

SEQ. ID. NO. 22 T T G G G C T T T A G T C T G G G C T A T G G C T C T A T G
SEQ. ID. NO. 23 G C T T A C G A A A C C A A G A G C G T G T C C A C T G A A

SEQ. ID. NO. 22 T T C A C C A A G A T C T G G T G G G T C C A C A C A G T C
SEQ. ID. NO. 23 A A G A T C A A T G A C C A C A G G G C C G T G G G C A T G

SEQ. ID. NO. 22 T T C A C G A A G A A G G A G G A G A A G A A G G A G T G G
SEQ. ID. NO. 23 G C T A T C T A C A A T G T C G C G G T C C T G T G T C T C

SEQ. ID. NO. 22 A G G A A G A C C C T A G A G C C C T G G A A A C T C T A T
SEQ. ID. NO. 23 A T C A C T G C T C C T G T G A C C A T G A T C C T T T C C

SEQ. ID. NO. 22 G C C A C T G T G G G C C T G C T G G T G G G C A T G G A T
SEQ. ID. NO. 23 A G T C A G C A G G A C G C A G C C T T T G C C T T T G C C

SEQ. ID. NO. 22 G T C C T G A C T C T T G C C A T C T G G C A G A T T G T G
SEQ. ID. NO. 23 T C T C T G G C C A T C G T G T T C T C T T C C T A C A T C

SEQ. ID. NO. 22 G A C C C C T T G C A C C G A A C C A T T G A G A C T T T T
SEQ. ID. NO. 23 A C T C T G G T T G T G C T C T T T G T G C C C A A G A T G

SEQ. ID. NO. 22 G C C A A G G A G G A A C C A A A G G A A G A C A T C G A T
SEQ. ID. NO. 23 C G C A G G C T G A T C A C C C G A G G G G A A T G G C A G

SEQ. ID. NO. 22 G T C T C C A T T C T G C C C C A G T T G G A G C A C T G C
SEQ. ID. NO. 23 T C T G A A A C G C A G G A C A C C A T G A A A A C A G G A

SEQ. ID. NO. 22 A G C T C C A A G A A G A T G A A T A C G T G G C T T G G C
SEQ. ID. NO. 23 T C A T C C A C C A A C A A C A A C G A G G A A G A G A A G

FIG. 6f

35/III

SEQ. ID. NO. 22 A T T T T C T A T G G T T A C A A G G G G C T G C T G C T G
SEQ. ID. NO. 23 T C C C G A C T G T T G G A G A A G G A A A A C C G A G A A

SEQ. ID. NO. 22 C T G C T G G G A A T C T T T C T T G C T T A C G A A A C C
SEQ. ID. NO. 23 C T G G A A A A G A T C A T C G C T G A G A A A G A G G A G

SEQ. ID. NO. 22 A A G A G C G T G T C C A C T G A A A A G A T C A A T G A C
SEQ. ID. NO. 23 C G C G T C T C T G A A C T G C G C C A T C A G C T C C A G

SEQ. ID. NO. 22 C A C A G G G C C G T G G G C A T G G C T A T C T A C A A T
SEQ. ID. NO. 23 T C T C G G C A G C A A C T C C G C T C A C G G C G C C A C

SEQ. ID. NO. 22 G T C G C G G T C C T G T G T C T C A T C A C T G C T C C T
SEQ. ID. NO. 23 C C C C C A A C A C C C C C A G A T C C C T C T G G G G G C

SEQ. ID. NO. 22 G T G A C C A T G A T C C T T T C C A G T C A G C A G G A C
SEQ. ID. NO. 23 C T T C C C A G G G G A C C C T C T G A G C C C C C T G A C

SEQ. ID. NO. 22 G C A G C C T T T G C C T T T G C C T C T C T G G C C A T C
SEQ. ID. NO. 23 C G G C T T A G C T G T G A T G G G A G T C G A G T A C A T

SEQ. ID. NO. 22 G T G T T C T C T T C C T A C A T C A C T C T G G T T G T G
SEQ. ID. NO. 23 T T G C T T T A C A A G

SEQ. ID. NO. 22 C T C T T T G T G C C C A A G A T G C G C A G G C T G A T C
SEQ. ID. NO. 23

SEQ. ID. NO. 22 A C C C G A G G G G A A T G G C A G T C T G A A A C G C A G
SEQ. ID. NO. 23

SEQ. ID. NO. 22 G A C A C C A T G A A A A C A G G A T C A T C C A C C A A C
SEQ. ID. NO. 23

SEQ. ID. NO. 22 A A C A A C G A G G A A G A G A A G T C C C G A C T G T T G
SEQ. ID. NO. 23

SEQ. ID. NO. 22 G A G A A G G A A A A C C G A G A A C T G G A A A A G A T C
SEQ. ID. NO. 23

FIG. 6g.

36/III

SEQ. ID. NO. 22 A T C G C T G A G A A A G A G G A G C G C G T C T C T G A A
SEQ. ID. NO. 23

SEQ. ID. NO. 22 C T G C G C C A T C A G C T C C A G T C T C G G C A G C A A
SEQ. ID. NO. 23

SEQ. ID. NO. 22 C T C C G C T C A C G G C G C C A C C C C C C A A C A C C C
SEQ. ID. NO. 23

SEQ. ID. NO. 22 C C A G A T C C C T C T G G G G G C C T T C C C A G G G G A
SEQ. ID. NO. 23

SEQ. ID. NO. 22 C C C T C T G A G C C C C C T G A C C G G C T T A G C T G T
SEQ. ID. NO. 23

SEQ. ID. NO. 22 G A T G G G A G T C G A G T A C A T T T G C T T T A C A A G
SEQ. ID. NO. 23

FIG. 6h.

37/III

SEQ. ID. NO. 24 M L L L L L V P L F L R P L G A G G A Q T P N A T S E G C Q
 SEQ. ID. NO. 25 M G P G G P C T P V G W P L P L L L V M A A G V A P V W A S

SEQ. ID. NO. 24 I I H P P W E G G I R Y R G L T R D Q V K A I N F L P V D Y
 SEQ. ID. NO. 25 H S P H L P R P H P R V P P H P S S E R R A V Y I G A L F P

SEQ. ID. NO. 24 E I E Y V C R G E R E V V G P K V R K C L A N G S W T D M D
 SEQ. ID. NO. 25 M S G G W P G G Q A C Q P A V E M A L E D V N S R R D I L P

SEQ. ID. NO. 24 T P S R C V R I C S K S Y L T L E N G K V F L T G G D L P A
 SEQ. ID. NO. 25 D Y E L K L I H H D S K C D P G Q A T K Y L Y E L L Y N D P

SEQ. ID. NO. 24 L D G A R V E F R C D P D F H L V G S S R S V C S Q G Q W S
 SEQ. ID. NO. 25 I K I I L M P G C S S V S T L V A E A A R M W N L I V L S Y

SEQ. ID. NO. 24 T P K P H C Q V N R T P H S E R R A V Y I G A L F P M S G G
 SEQ. ID. NO. 25 G S S S P A L S N R Q R F P T F F R T H P S A T L H N P T R

SEQ. ID. NO. 24 W P G G Q A C Q P A V E M A L E D V N S R R D I L P D Y E L
 SEQ. ID. NO. 25 V K L F E K W G W K K I A T I Q Q T T E V F T S T L D D L E

SEQ. ID. NO. 24 K L I H H D S K C D P G Q A T K Y L Y E L L Y N D P I K I I
 SEQ. ID. NO. 25 E R V K E A G I E I T F R Q S F F S D P A V P V K N L K R Q

SEQ. ID. NO. 24 L M P G C S S V S T L V A E A A R M W N L I V L S Y G S S S
 SEQ. ID. NO. 25 D A R I I V G L F Y E T E A R K V F C E V Y K E R L F G K K

SEQ. ID. NO. 24 P A L S N R Q R F P T F F R T H P S A T L H N P T R V K L F
 SEQ. ID. NO. 25 Y V W F L I G W Y A D N W F K T Y D P S I N C T V E E M T E

SEQ. ID. NO. 24 E K W G W K K I A T I Q Q T T E V F T S T L D D L E E R V K
 SEQ. ID. NO. 25 A V E G H I T T E I V M L N P A N T R S I S N M T S Q E F V

SEQ. ID. NO. 24 E A G I E I T F R Q S F F S D P A V P V K N L K R Q D A R I
 SEQ. ID. NO. 25 E K L T K R L K R H P E E T G G F Q E A P L A Y D A I W A L

FIG. 7a

38/III

SEQ. ID. NO. 24 I V G L F Y E T E A R K V F C E V Y K E R L F G K K Y V W F
 SEQ. ID. NO. 25 A L A L N K T S G G G G R S G V R L E D F N Y N N Q T I T D

SEQ. ID. NO. 24 L I G W Y A D N W F K T Y D P S I N C T V E E M T E A V E G
 SEQ. ID. NO. 25 Q I Y R A M N S S S F E G V S G H V V F D A S G S R M A W T

SEQ. ID. NO. 24 H I T T E I V M L N P A N T R S I S N M T S Q E F V E K L T
 SEQ. ID. NO. 25 L I E Q L Q G G S Y K K I G Y Y D S T K D D L S W S K T D K

SEQ. ID. NO. 24 K R L K R H P E E T G G F Q E A P L A Y D A I W A L A L A L
 SEQ. ID. NO. 25 W I G G S P P A D Q I L V I K T F R F L S Q K L F I S V S V

SEQ. ID. NO. 24 N K T S G G G G R S G V R L E D F N Y N N Q T I T D Q I Y R
 SEQ. ID. NO. 25 L S S L G I V L A V V C L S F N I Y N S H V R Y I O N S O P

SEQ. ID. NO. 24 A M N S S S F E G V S G H V V F D A S G S R M A W T L I E Q
 SEQ. ID. NO. 25 N L N N L T A V G C S L A L A A V F P L G L D G Y H I G R S

SEQ. ID. NO. 24 L Q G G S Y K K I G Y Y D S T K D D L S W S K T D K W I G G
 SEQ. ID. NO. 25 Q F P F V C Q A R L W L L G L G F S L G Y G S M F T K I W W

SEQ. ID. NO. 24 S P P A D Q I L V I K T F R F L S Q K L F I S V S V L S S L
 SEQ. ID. NO. 25 V H T V F T K K E E K K E W R K T L E P W K L Y A T V G L L

SEQ. ID. NO. 24 G I V L A V V C L S F N I Y N S H V R Y I O N S O P N L N N
 SEQ. ID. NO. 25 V G M D V L T L A I W Q I V D P L H R T I E T F A K E E P K

SEQ. ID. NO. 24 L T A V G C S L A L A A V F P L G L D G Y H I G R S Q F P F
 SEQ. ID. NO. 25 E D I D V S I L P Q L E H C S S K K M N T W L G I F Y G Y K

SEQ. ID. NO. 24 V C Q A R L W L L G L G F S L G Y G S M F T K I W W V H T V
 SEQ. ID. NO. 25 G L L L L L G I F L A Y E T K S V S T E K I N D H R A V G M

SEQ. ID. NO. 24 F T K K E E K K E W R K T L E P W K L Y A T V G L L V G M D
 SEQ. ID. NO. 25 A I Y N V A V L C L I T A P V T M I L S S Q Q D A A F A F A

SEQ. ID. NO. 24 V L T L A I W Q I V D P L H R T I E T F A K E E P K E D I D
 SEQ. ID. NO. 25 S L A I V F S S Y I T L V V L F V P K M R R L I T R G E W O

FIG. 7b.

39/III

SEQ. ID. NO. 24 V S I L P Q L E H C S S K K M N T W L G I F Y G Y K G L L L
SEQ. ID. NO. 25 S E T Q D T M K T G S S T N N N E E E K S R L L E K E N R E

SEQ. ID. NO. 24 L L G I F L A Y E T K S V S T E K I N D H R A V G M A I Y N
SEQ. ID. NO. 25 L E K I I A E K E E R V S E L R H Q L Q S R Q Q L R S R R H

SEQ. ID. NO. 24 V A V L C L I T A P V T M I L S S Q O D A A F A F A S L A I
SEQ. ID. NO. 25 P P T P P D P S G G L P R G P S E P P D R L S C D G S R V H

SEQ. ID. NO. 24 V F S S Y I T L V V L F V P K M R R L I T R G E W Q S E T Q
SEQ. ID. NO. 25 L L Y K

SEQ. ID. NO. 24 D T M K T G S S T N N N E E E K S R L L E K E N R E L E K I
SEQ. ID. NO. 25

SEQ. ID. NO. 24 I A E K E E R V S E L R H Q L Q S R Q Q L R S R R H P P T P
SEQ. ID. NO. 25

SEQ. ID. NO. 24 P D P S G G L P R G P S E P P D R L S C D G S R V H L L Y K
SEQ. ID. NO. 25

FIG. 7c.

40/III

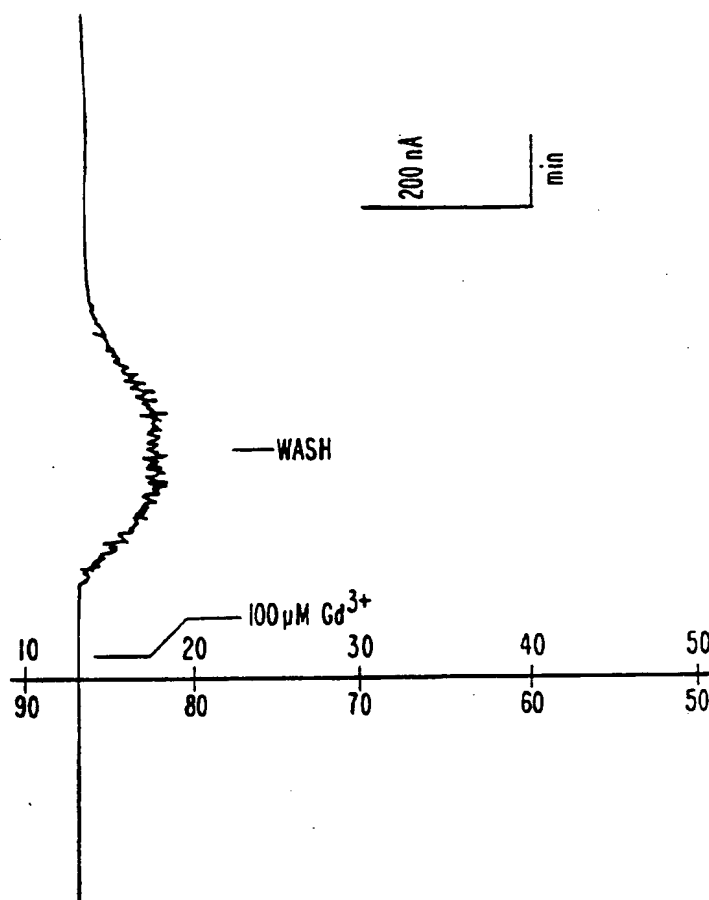


FIG. 8.

41/III

ClustalW Formatted Alignments

SEQ. ID. NO. 38 A T G G T A T G C G A G G G A A A G C G A T C A G
 SEQ. ID. NO. 34 A T G G G A T C G C T G C T T G C G C T C C C G G
 SEQ. ID. NO. 30 A T G G C A T T T T A T A G C T G C T G C T G G G
 SEQ. ID. NO. 26 A T G G G A T C G C T G C T T G C G C T C C T G G

SEQ. ID. NO. 38 C C T C T T G C C C T T G T T T C T T C C T C T T
 SEQ. ID. NO. 34 C A C T G C T G C T G C T G T G G G G T G C T G T
 SEQ. ID. NO. 30 T C C T C T T G G C A C T C A C C T G G C A C A C
 SEQ. ID. NO. 26 C A C T G C T G C C G C T G T G G G G T G C T G T

SEQ. ID. NO. 38 G A C C G C C A A G T T C T A C T G G A T C C T C
 SEQ. ID. NO. 34 G G C T G A G G G C C C A G C C A A G A A A G G T G
 SEQ. ID. NO. 30 C T C T G C C T A C G G G C C A G A C C A G C G A
 SEQ. ID. NO. 26 G G C T G A G G G C C C A G C C A A G A A A G G T G

SEQ. ID. NO. 38 A C A A T G A T G C A A A G A A C T C A C A G C C
 SEQ. ID. NO. 34 C T G A C C C T G G A G G G A G A C T T G G T G C
 SEQ. ID. NO. 30 G C C C A A A A G A A A G G G G G A C A T T A T C C
 SEQ. ID. NO. 26 C T G A C C C T G G A G G G A G A C T T G G T G C

SEQ. ID. NO. 38 A G G A G T A T G C C C A T T C C A T A C G G G T
 SEQ. ID. NO. 34 T G G G T G G G C T G T T C C C A G T G C A C C A
 SEQ. ID. NO. 30 T T G G G G G G C T C T T T C C T A T T C A T T T
 SEQ. ID. NO. 26 T G G G T G G G C T G T T C C C A G T G C A C C A

SEQ. ID. NO. 38 G G A T G G G G A C A T T A T T T T G G G G G G T
 SEQ. ID. NO. 34 G A A G G G C G G C C C A G C A G A G G A C T G T
 SEQ. ID. NO. 30 T G G A G T A G C A G C T A A A G A T C A A G A T
 SEQ. ID. NO. 26 G A A G G G C G G C C C A G C A G A G G A C T G T

SEQ. ID. NO. 38 C T C T T C C C T G T C C A C G C A A A G G G A G
 SEQ. ID. NO. 34 G G T C C T G T C A A T G A G C A C C G T G G C A
 SEQ. ID. NO. 30 C T C A A A T C A A G G C C G G A G T C T G T G G
 SEQ. ID. NO. 26 G G T C C T G T C A A T G A G C A C C G T G G C A

SEQ. ID. NO. 38 A G A G A G G G G T G C C T T G T G G G G A G C T
 SEQ. ID. NO. 34 T C C A G C G C C T G G A G G C C A T G C T T T T
 SEQ. ID. NO. 30 A A T G T A T C A G G T A T A A T T T C C G T G G
 SEQ. ID. NO. 26 T C C A G C G C C T G G A G G C C A T G C T T T T

FIG. 9a.

42/III

SEQ. ID. NO. 38 G A A G A A G G A A A G G G A T T C A C A G A
SEQ. ID. NO. 34 T G C A C T G G A C C G C A T C A A C C G T G A C
SEQ. ID. NO. 30 G T T T C G C T G G T T A C A G G C T A T G A T A
SEQ. ID. NO. 26 T G C A C T G G A C C G C A T C A A C C G T G A C

SEQ. ID. NO. 38 C T G G A G G C C A T G C T T T A T G C A A T T G
SEQ. ID. NO. 34 C C G C A C C T G C T G C C T G G C G T G C G C C
SEQ. ID. NO. 30 T T T G C C A T A G A G G A G A T A A A C A G C A
SEQ. ID. NO. 26 C C G C A C C T G C T G C C T G G C G T G C G C C

SEQ. ID. NO. 38 A C C A G A T T A A C A A G G A C C C T G A T C T
SEQ. ID. NO. 34 T G G G T G C A C A C A T C C T C G A C A G T T G
SEQ. ID. NO. 30 G C C C A G C C C T T C T T C C C A A C T T G A C
SEQ. ID. NO. 26 T G G G T G C A C A C A T C C T C G A C A G T T G

SEQ. ID. NO. 38 C C T T T C C A A C A T C A C T C T G G G T G T C
SEQ. ID. NO. 34 C T C C A A G G A C A C A C A T G C G C T G G A G
SEQ. ID. NO. 30 G C T G G G A T A C A G G A T A T T T G A C A C T
SEQ. ID. NO. 26 C T C C A A G G A C A C A C A T G C G C T G G A G

SEQ. ID. NO. 38 C G C A T C C T C G A C A C G T G C T C T A G G G
SEQ. ID. NO. 34 C A G G C A C T G G A C T T T G T G C G T G C C T
SEQ. ID. NO. 30 T G C A A C A C C G T T T C T A A G G C C T T G G
SEQ. ID. NO. 26 C A G G C A C T G G A C T T T G T G C G T G C C T

SEQ. ID. NO. 38 A C A C C T A T G C T T T G G A G C A G T C T C T
SEQ. ID. NO. 34 C A C T C A G C C G T G G T G C T G A T G G C T C
SEQ. ID. NO. 30 A A G C C A C C C T G A G T T T T G T T G C T C A
SEQ. ID. NO. 26 C A C T C A G C C G T G G T G C T G A T G G A T C

SEQ. ID. NO. 38 A A C A T T C G T G C A G G C A T T A A T A G A G
SEQ. ID. NO. 34 A C G C C A C A T C T G C C C C G A C G G C T C T
SEQ. ID. NO. 30 A A A C A A A A T T G A T T C T T T G A A C C T T
SEQ. ID. NO. 26 A C G C C A C A T C T G C C C C G A C G G C T C T

SEQ. ID. NO. 38 A A A G A T G C T T C G G A T G T G A A G T G T G
SEQ. ID. NO. 34 T A T G C G A C C C A T G G T G A T G C T C C C A
SEQ. ID. NO. 30 G A T G A G T T C T G C A A C T G C T C A G A G C
SEQ. ID. NO. 26 T A T G C G A C C C A T G G T G A T G C T C C C A

FIG. 9b.

43/III

SEQ. ID. NO. 38 C T A A T G G A G A T C C A C C C A T T T T C A C
SEQ. ID. NO. 34 C T G C C A T C A C T G G T G T T A T T G G C G G
SEQ. ID. NO. 30 A C A T T C C C T C T A C G A T T G C T G T G G T
SEQ. ID. NO. 26 C T G C C A T C A C T G G T G T T A T T G G C G G

SEQ. ID. NO. 38 C A A G C C C G A C A A G A T T T C T G G C G T C
SEQ. ID. NO. 34 T T C C T A C A G T G A T G T C T C C A T C C A G
SEQ. ID. NO. 30 G G G A G C A A C T G G C T C A G G C G T C T C C
SEQ. ID. NO. 26 T T C C T A C A G T G A T G T C T C C A T C C A G

SEQ. ID. NO. 38 A T A G G T G C T G C A G C A A G C T C C G T G T
SEQ. ID. NO. 34 G T G G C C A A C C T C T T G A G G C T A T T T C
SEQ. ID. NO. 30 A C G G C A G T G G C A A A T C T G C T G G G G C
SEQ. ID. NO. 26 G T G G C C A A C C T C T T G A G G C T A T T T C

SEQ. ID. NO. 38 C C A T C A T G G T T G C T A A C A T T T T A A G
SEQ. ID. NO. 34 A G A T C C C A C A G A T T A G C T A C G C C T C
SEQ. ID. NO. 30 T C T T C T A C A T T C C C C A G G T C A G T T A
SEQ. ID. NO. 26 A G A T C C C A C A G A T T A G C T A C G C C T C

SEQ. ID. NO. 38 A C T T T T T A A G A T A C C T C A A A T C A G C
SEQ. ID. NO. 34 T A C C A G T G C C A A G C T G A G T G A C A A G
SEQ. ID. NO. 30 T G C C T C C T C C A G C A G A C T C C T C A G C
SEQ. ID. NO. 26 T A C C A G T G C C A A G C T G A G T G A C A A G

SEQ. ID. NO. 38 T A T G C A T C C A C A G C C C C A G A G C T A A
SEQ. ID. NO. 34 T C C C G C T A T G A C T A C T T T G C C C G C A
SEQ. ID. NO. 30 A A C A A G A A T C A A T T C A A G T C T T T C C
SEQ. ID. NO. 26 T C C C G C T A T G A C T A C T T T G C C C G C A

SEQ. ID. NO. 38 G T G A T A A C A C C A G G T A T G A C T T T T T
SEQ. ID. NO. 34 C A G T G C C T C C T G A C T T C T T C C A A G C
SEQ. ID. NO. 30 T C C G A A C C A T C C C C A A T G A T G A G C A
SEQ. ID. NO. 26 C A G T G C C T C C T G A C T T C T T C C A A G C

SEQ. ID. NO. 38 C T C T C G A G T G G T T C C G C C T G A C T C C
SEQ. ID. NO. 34 C A A G G C C A T G G C T G A G A T T C T C C G C
SEQ. ID. NO. 30 C C A G G C C A C T G C C A T G G C A G A C A T C
SEQ. ID. NO. 26 C A A G G C C A T G G C T G A G A T T C T C C G C

FIG. 9c.

44/III

SEQ. ID. NO. 38 T A C C A A G C C C A A G C C A T G G T G G A C A
SEQ. ID. NO. 34 T T C T T C A A C T G G A C C T A T G T G T C C A
SEQ. ID. NO. 30 A T C G A G T A T T T C C G C T G G A A C T G G G
SEQ. ID. NO. 26 T T C T T C A A C T G G A C C T A T G T G T C C A

SEQ. ID. NO. 38 T C G T G A C A G C A C T G G G A T G G A A T T A
SEQ. ID. NO. 34 C T G T G G C G T C T G A G G G C G A C T A T G G
SEQ. ID. NO. 30 T G G G C A C A A T T G C A G C T G A T G A C G A
SEQ. ID. NO. 26 C T G A G G C C T C T G A G G G C G A C T A T G G

SEQ. ID. NO. 38 T G T T T C G A C A C T G G C T T C T G A G G G G
SEQ. ID. NO. 34 C G A G A C A G G C A T T G A G G C C T T T G A G
SEQ. ID. NO. 30 C T A T G G G C G G C C G G G A T T G A G A A A
SEQ. ID. NO. 26 C G A G A C A G G C A T T G A G G C C T T T G A G

SEQ. ID. NO. 38 A A C T A T G G T G A G A G C G G T G T G G A G G
SEQ. ID. NO. 34 C T A G A G G C T C G T G C C C G C A A C A T C T
SEQ. ID. NO. 30 T T C C G A G A G G A A G C T G A G G A A A G G G
SEQ. ID. NO. 26 C T A G A G G C T C G T G C C C G C A A C A T C T

SEQ. ID. NO. 38 C C T T C A C C C A G A T C T C G A G G G A G A T
SEQ. ID. NO. 34 G T G T G G C C A C C T C G G A G A A A G T G G G
SEQ. ID. NO. 30 A T A T C T G C A T C G A C T T C A G T G A A C T
SEQ. ID. NO. 26 G T G T G G C C A C C T C G G A G A A A G T G G G

SEQ. ID. NO. 38 T G G T G G T G T T T G C A T T G C T C A G T C A
SEQ. ID. NO. 34 C C G T G C C A T G A G C C G C G C G G C C T T T
SEQ. ID. NO. 30 C A T C T C C C A G T A C T C T G A T G A G G A A
SEQ. ID. NO. 26 C C G T G C C A T G A G C C G C G C G G C C T T T

SEQ. ID. NO. 38 C A G A A A A T C C C A C G T G A A C C A A G A C
SEQ. ID. NO. 34 G A G G G T G T G G T G C G A G C C C T G C T G C
SEQ. ID. NO. 30 G A G A T C C A G C A T G T G G T A G A G G T G A
SEQ. ID. NO. 26 G A G G G T G T G G T G C G A G C C C T G C T G C

SEQ. ID. NO. 38 C T G G A G A A T T T G A A A A A A T T A T C A A
SEQ. ID. NO. 34 A G A A G C C C A G T G C C C G C G T G G C T G T
SEQ. ID. NO. 30 T T C A A A A T T C C A C G G C C A A A G T C A T
SEQ. ID. NO. 26 A G A A G C C C A G T G C C C G C G T G G C T G T

FIG. 9d.

45/III

SEQ. ID. NO. 38 A C G C C T G C T A G A A A C A C C T A A T G C T
SEQ. ID. NO. 34 C C T G T T C A C C C G T T C T G A G G A T G C C
SEQ. ID. NO. 30 C G T G G T T T T T C T C C A G T G G C C C A G A T
SEQ. ID. NO. 26 C C T G T T C A C C C G T T C T G A G G A T G C C

SEQ. ID. NO. 38 C G A G C A G T G A T T A T G T T T G C C A A T G
SEQ. ID. NO. 34 C G G G A G C T G C T T G C T G C C A G C C A G C
SEQ. ID. NO. 30 C T T G A G C C C C T C A T C A A G G A G A T T G
SEQ. ID. NO. 26 C G G G A G C T G C T T G C T G C C A G C C A G C

SEQ. ID. NO. 38 A G G A T G A C A T C A G G A G G A T A T T G G A
SEQ. ID. NO. 34 G C C T C A A T G C C A G C T T C A C C T G G G T
SEQ. ID. NO. 30 T C C G G C G C A A T A T C A C G G G C A A G A T
SEQ. ID. NO. 26 G C C T C A A T G C C A G C T T C A C C T G G G T

SEQ. ID. NO. 38 A G C A G C A A A A A A A C T A A A C C A A A G T
SEQ. ID. NO. 34 G G C C A G T G A T G G T T G G G G G G C C C T G
SEQ. ID. NO. 30 C T G G C T G G C C A G C G A G G C C T G G G C C
SEQ. ID. NO. 26 G G C C A G T G A T G G T T G G G G G G C C C T G

SEQ. ID. NO. 38 G G G C A T T T T C T C T G G A T T G G C T C A G
SEQ. ID. NO. 34 G A G A G T G T G G T G G C A G G C A G T G A G G
SEQ. ID. NO. 30 A G C T C C T C C C T G A T C G C C A T G C C T C
SEQ. ID. NO. 26 G A G A G T G T G G T G G C A G G C A G T G A G G

SEQ. ID. NO. 38 A T A G T T G G G G A T C C A A A A T A G C A C C
SEQ. ID. NO. 34 G G G C T G C T G A G G G T G C T A T C A C C A T
SEQ. ID. NO. 30 A G T A C T T C C A C G T G G T T G G C G G C A C
SEQ. ID. NO. 26 G G G C T G C T G A G G G T G C T A T C A C C A T

SEQ. ID. NO. 38 T G T C T A T C A G C A A G A G G A G A T T G C A
SEQ. ID. NO. 34 C G A G C T G G C C T C C T A C C C C A T C A G T
SEQ. ID. NO. 30 C A T T G G A T T C G C T C T G A A G G C T G G G
SEQ. ID. NO. 26 C G A G C T G G C C T C C T A C C C C A T C A G T

SEQ. ID. NO. 38 G A A G G G G C T G T G A C A A T T T T G C C C A
SEQ. ID. NO. 34 G A C T T T G C C T C C T A C T T C C A G A G C C
SEQ. ID. NO. 30 C A G A T C C C A G G C T T C C G G G A A T T C C
SEQ. ID. NO. 26 G A C T T T G C C T C C T A C T T C C A G A G C C

FIG. 9e.

SUBSTITUTE SHEET (RULE 26)

46/III

SEQ. ID. NO. 38 A A C G A G C A T C A A T T G A T G G A T T T G A
SEQ. ID. NO. 34 T G G A C C C T T G G A A C A A C A G C C G G A A
SEQ. ID. NO. 30 T G A A G A A G G T C C A T C C C A G G A A G T C
SEQ. ID. NO. 26 T G G A C C C T T G G A A C A A C A G C C G G A A

SEQ. ID. NO. 38 T C G A T A C T T T A G A A G C C G A A C T C T T
SEQ. ID. NO. 34 C C C C T G G T T C C G T G A A T T C T G G G A G
SEQ. ID. NO. 30 T G T C C A C A A T G G T T T T G C C A A G G A G
SEQ. ID. NO. 26 C C C C T G G T T C C G T G A A T T C T G G G A G

SEQ. ID. NO. 38 G C C A A T A A T C G A A G A A A T G T G T G G T
SEQ. ID. NO. 34 C A G A G G T T C C G C T G C A G C T T C C G G C
SEQ. ID. NO. 30 T T T T G G G A A G A A A C A T T T A A C T G C C
SEQ. ID. NO. 26 C A G A G G T T C C G C T G C A G C T T C C G G C

SEQ. ID. NO. 38 T T G C A G A A T T C T G G G A G G A G A A T T T
SEQ. ID. NO. 34 A G C G A G A C T G C G C A G C C C A C T C T C T
SEQ. ID. NO. 30 A C C T C C A A G A A G G T G C A A A A G G A C C
SEQ. ID. NO. 26 A G C G A G A C T G C G C A G C C C A C T C T C T

SEQ. ID. NO. 38 T G G C T G C A A G T T A G G A T C A C A T G G G
SEQ. ID. NO. 34 C C G G G C T G T G C C C T T T G A G C A G G A G
SEQ. ID. NO. 30 T T T A C C T G T G G A C A C C T T T C T G A G A
SEQ. ID. NO. 26 C C G G G C T G T G C C C T T T G A A C A G G A G

SEQ. ID. NO. 38 A A A A G G A A C A G T C A T A T A A A G A A A T
SEQ. ID. NO. 34 T C C A A G A T C A T G T T T G T G G T C A A T G
SEQ. ID. NO. 30 G G T C A C G A A G A A A G T G G C G A C A G G T
SEQ. ID. NO. 26 T C C A A G A T C A T G T T T G T G G T C A A T G

SEQ. ID. NO. 38 G C A C A G G G C T G G A G C G A A T T G C T C G
SEQ. ID. NO. 34 C A G T G T A C G C C A T G G C C C A T G C G C T
SEQ. ID. NO. 30 T T A G C A A C A G C T C G A C A G C C T T C C G
SEQ. ID. NO. 26 C A G T G T A C G C C A T G G C C C A T G C G C T

SEQ. ID. NO. 38 G G A T T C A T C T T A T G A A C A G G A A G G A
SEQ. ID. NO. 34 C C A C A A C A T G C A C C G T G C C C T C T G C
SEQ. ID. NO. 30 A C C C C T C T G T A C A G G G G A T G A G A A C
SEQ. ID. NO. 26 C C A C A A C A T G C A C C G T G C C C T C T G C

FIG. 9f

SUBSTITUTE SHEET (RULE 26)

47/III

SEQ. ID. NO. 38 A A G G T C C A A T T T G T A A T T G A T G C T G
SEQ. ID. NO. 34 C C C A A C A C C A C C C G G C T C T G T G A C G
SEQ. ID. NO. 30 A T C A G C A G T G T C G A G A C C C C T T A C A
SEQ. ID. NO. 26 C C C A A C A C C A C C C G G C T C T G T G A C G

SEQ. ID. NO. 38 T A T A T T C C A T G G C T T A C G C C C T G C A
SEQ. ID. NO. 34 C G A T G C G G C C A G T T A A C G G G C G C C G
SEQ. ID. NO. 30 T A G A T T A C A C G C A T T T A C G G A T A T C
SEQ. ID. NO. 26 C G A T G C G G C C A G T T A A C G G G C G C C G

SEQ. ID. NO. 38 C A A T A T G C A C A A A G A T C T C T G C C C T
SEQ. ID. NO. 34 C C T C T A C A A G G A C T T T G T G C T C A A C
SEQ. ID. NO. 30 C T A C A A T G T G T A C T T A G C A G T C T A C
SEQ. ID. NO. 26 C C T C T A C A A G G A C T T T G T G C T C A A C

SEQ. ID. NO. 38 G G A T A C A T T T G G C C T T T G T C C A C G A A
SEQ. ID. NO. 34 G T C A A G T T T T G A T G C C C C C T T T C G C C
SEQ. ID. NO. 30 T C C A T T G C C C A C G C C T T G C A A G A T A
SEQ. ID. NO. 26 G T C A A G T T T T G A T G C C C C C T T T C G C C

SEQ. ID. NO. 38 T G A G T A C C A T T G A T G G G A A A G A G C T
SEQ. ID. NO. 34 C A G C T G A C A C C C A C A A T G A G G T C C G
SEQ. ID. NO. 30 T A T A T A C C T G C T T A C C T G G G A G A G G
SEQ. ID. NO. 26 C A G C T G A C A C C C A C A A T G A G G T C C G

SEQ. ID. NO. 38 A C T T G G T T A T A T T C G G G C T G T A A A T
SEQ. ID. NO. 34 C T T T G A C C G C T T T G G T G A T G G T A T T
SEQ. ID. NO. 30 G C T C T T C A C C A A T G G C T C C T G T G C A
SEQ. ID. NO. 26 C T T T G A C C G C T T T G G T G A T G G T A T T

SEQ. ID. NO. 38 T T T A A T G G C A G T G C T G G C A C T C C T G
SEQ. ID. NO. 34 G G C C G C T A C A A C A T C T T C A C C T A T C
SEQ. ID. NO. 30 G A C A T C A A G A A A G T T G A G G C G T G G C
SEQ. ID. NO. 26 G G C C G C T A C A A C A T C T T C A C C T A T C

SEQ. ID. NO. 38 T C A C T T T T A A T G A A A A C G G A G A T G C
SEQ. ID. NO. 34 T G C G T G C A G G C A G T G G G C G C T A T C G
SEQ. ID. NO. 30 A G G T C C T G A A G C A C C T A C G G C A T C T
SEQ. ID. NO. 26 T G C G T G C A G G C A G T G G G C G C T A T C G

FIG. 9g.

48/III

SEQ. ID. NO. 38 T C C T G G A C G T T A T G A T A T C T T C C A G
SEQ. ID. NO. 34 C T A C C A G A A G G T G G G C T A C T G G G C A
SEQ. ID. NO. 30 A A A C T T T A C A A A C A A T A T G G G G G A G
SEQ. ID. NO. 26 C T A C C A G A A G G T G G G C T A C T G G G C A

SEQ. ID. NO. 38 T A T C A A A T A A C C A A C A A A A G C A C A G
SEQ. ID. NO. 34 G A A G G C T T T G A C T C T G G A C A C C A G C C
SEQ. ID. NO. 30 C A G G T G A C C T T T G A T G A G T G T G G T G
SEQ. ID. NO. 26 G A A G G C T T G A C T C T G G A C A C C A G C C

SEQ. ID. NO. 38 A G T A C A A A G T C A T C G G C C A C T G G A C
SEQ. ID. NO. 34 T C A T C C C A T G G G C C T C A C C C T C A G C
SEQ. ID. NO. 30 A C C T G G T G G G G A A C T A T T C C A T C A T
SEQ. ID. NO. 26 T C A T C C C A T G G G C C T C A C C G T C A G C

SEQ. ID. NO. 38 C A A T C A G C T T C A T C T A A A A G T G G A A
SEQ. ID. NO. 34 C G G C C C C C T G C C C G C C T C T C G C T G C
SEQ. ID. NO. 30 C A A C T G G C A C C T C T C C C C A G A G G A T
SEQ. ID. NO. 26 C G G C C C C C T G G C C G C C T C T C G C T G C

SEQ. ID. NO. 38 G A C A T G C A G T G G G C T C A T A G A G A A C
SEQ. ID. NO. 34 A G T G A G C C C T G C C T C C A G A A T G A G G
SEQ. ID. NO. 30 G G C T C C A T C G T G T T T A A G G A A G T C G
SEQ. ID. NO. 26 A G T G A G C C C T G C C T C C A G A A T G A G G

SEQ. ID. NO. 38 A T A C T C A C C C G G C G T C T G T C T G C A G
SEQ. ID. NO. 34 T G A A G A G T G T G C A G C C G G G C G A A G T
SEQ. ID. NO. 30 G G T A T T A C A A C G T C T A T G C C A A G A A
SEQ. ID. NO. 26 T G A A G A G T G T G C A G C C G G G C G A A G T

SEQ. ID. NO. 38 C C T G C C G T G T A A G C C A G G G G A G A G G
SEQ. ID. NO. 34 C T G C T G C T G G C T C T G C A T T C C G T G C
SEQ. ID. NO. 30 G G G A G A A A G A C T C T T C A T C A A C G A G
SEQ. ID. NO. 26 C T G C T G C T G G C T C T G C A T T C C G T G C

SEQ. ID. NO. 38 A A G A A A A C G G T G A A A G G G G T C C C T T
SEQ. ID. NO. 34 C A G C C C T A T G A G T A C C G A T T G G A C G
SEQ. ID. NO. 30 G A G A A A A T C C T G T G G A G T G G G T T C T
SEQ. ID. NO. 26 C A G C C C T A T G A G T A C C G A T T G G A C G

FIG. 9h.

SUBSTITUTE SHEET (RULE 26)

49/III

SEQ. ID. NO. 38 G C T G C T G G C A C T G T G A A C G C T G T G A
SEQ. ID. NO. 34 A A T T C A C T T G C G C T G A T T G T G G C C T
SEQ. ID. NO. 30 C C A G G G A G G T G C C C T T C T C C A A C T G
SEQ. ID. NO. 26 A A T T C A C T T G C G C T G A T T G T G G C C T

SEQ. ID. NO. 38 A G G T T A C A A C T A C C A G G T G G A T G A G
SEQ. ID. NO. 34 G G G C T A C T G G C C C A A T G C C A G C C T G
SEQ. ID. NO. 30 C A G C C G A G A C T G C C T G G C A G G G A C C
SEQ. ID. NO. 26 G G G C T A C T G G C C C A A T G C C A G C C T G

SEQ. ID. NO. 38 C T G T C C T G T G A A C T T T G C C C T C T G G
SEQ. ID. NO. 34 A C T G G C T G C T T C G A A C T G C C C C A G G
SEQ. ID. NO. 30 A G G A A A G G G A T C A T T G A G G G G G A G C
SEQ. ID. NO. 26 A C T G G C T G C T T C G A A C T G C C C C A G G

SEQ. ID. NO. 38 A T C A G A G A C C C A A C A T G A A C C G C A C
SEQ. ID. NO. 34 A G T A C A T C C G C T G G G G C G A T G C C T G
SEQ. ID. NO. 30 C C A C C T G C T G C T T T G A G T G T G T G G A
SEQ. ID. NO. 26 A G T A C A T C C G C T G G G G C G A T G C C T G

SEQ. ID. NO. 38 A G G C T G C C A G C T T A T C C C C A T C A T C
SEQ. ID. NO. 34 G G C T G T G G G A C C T G T C A C C A T C G C C
SEQ. ID. NO. 30 G T G T C C T G A T G G G G A G T A T A G T G A T
SEQ. ID. NO. 26 G G C T G T G G G A C C T G T C A C C A T C G C C

SEQ. ID. NO. 38 A A A T T G G A G T G G C A T T C T C C C T G G G
SEQ. ID. NO. 34 T G C C T C G G T G C C C T G G C C A C C C T C T
SEQ. ID. NO. 30 G A G A C A G A T G C C A G T G C C T G T A A C A
SEQ. ID. NO. 26 T G C C T C G G T G C C C T G G C C A C C C T G T

SEQ. ID. NO. 38 C T G T G G T G C C T G T G T T T G T T G C A A T
SEQ. ID. NO. 34 T T G T G C T G G G T G T C T T T G T G C G G C A
SEQ. ID. NO. 30 A G T G C C C A G A T G A C T T T C T G G T C C A A
SEQ. ID. NO. 26 T T G T G C T G G G T G T C T T T G T G C G G C A

SEQ. ID. NO. 38 A T T G G G A A T C A T C G C C A C C A C C T T T
SEQ. ID. NO. 34 C A A T G C C A C A C C A G T G G T C A A G G C C
SEQ. ID. NO. 30 T G A G A A C C A C A C C T C C T G C T T C G A A
SEQ. ID. NO. 26 C A A T G C C A C A C C A G T G G T C A A G G C C

FIG. 9i.

SUBSTITUTE SHEET (RULE 26)

50/III

SEQ. ID. NO. 38 GTGATCGTGACCTTTGTCCGCTATA
SEQ. ID. NO. 34 TCAGGTCGGGAGCTCTGCTACATCC
SEQ. ID. NO. 30 CTGCCCCAGGAGTACATCCGCTGGG
SEQ. ID. NO. 26 TCAGGTCGGGAGCTCTGCTACATCC

SEQ. ID. NO. 38 ATGACACACCTATCGTGAGGGCTTC
SEQ. ID. NO. 34 TGCTGGGTGGGTGTCCTCCTGCTA
SEQ. ID. NO. 30 GCGATGCCCTGGGGCTGTGGGACCTGT
SEQ. ID. NO. 26 TGCTGGGTGGGTGTCCTCCTGCTA

SEQ. ID. NO. 38 AGGACGCGAACTTAGTTACGTGCTC
SEQ. ID. NO. 34 CTGCATGACCTTTCATCTTTCATTGCC
SEQ. ID. NO. 30 CACCATCGCCTGCTCCTCGGTGCCCTG
SEQ. ID. NO. 26 CTGCATGACCTTTCATCTTTCATTGCC

SEQ. ID. NO. 38 CTAACGGGGATTTTTCTCTGTATT
SEQ. ID. NO. 34 AAGCCATCCACGGGCAGTGTGTACCT
SEQ. ID. NO. 30 GCCACCCTGTTTGTGCTGGGTGCT
SEQ. ID. NO. 26 AAGCCATCCACGGGCAGTGTGTACCT

SEQ. ID. NO. 38 CAATCACGTTTTTTAATGATTGACAGC
SEQ. ID. NO. 34 TACGGCGTCTTTGGTTTGGGGCACTGC
SEQ. ID. NO. 30 TTGTGCGGGCACAATGCCACACCAGT
SEQ. ID. NO. 26 TACGGCGTCTTTGGTTTGGGGCACTGC

SEQ. ID. NO. 38 ACCAGATACAATCATATGCTCCTTTC
SEQ. ID. NO. 34 CTTCTCTGTCTGTCTACTCAGCCCTG
SEQ. ID. NO. 30 GGTCAAGGCCCTCAGGTCGGGAGCTC
SEQ. ID. NO. 26 CTTCTCTGTCTGTCTACTCAGCCCTG

SEQ. ID. NO. 38 CGACGGGTCTTTCCTAGGACTTTGGCA
SEQ. ID. NO. 34 CTCACCAAGACCAACCGCATTTGCAC
SEQ. ID. NO. 30 TGCTACATCCTGCTGGGTGGTGTCT
SEQ. ID. NO. 26 CTCACCAAGACCAACCGCATTTGCAC

SEQ. ID. NO. 38 TGTGTTTTCAGCTATGACAGCCCTTCT
SEQ. ID. NO. 34 GCATCTTTCGGTGGGGGCCCGGGAGGG
SEQ. ID. NO. 30 TCCTCTGCTACTGCATGACCTTTCAT
SEQ. ID. NO. 26 GCATCTTTCGGTGGGGGCCCGGGAGGG

FIG. 9j

SUBSTITUTE SHEET (RULE 26)

51/III

SEQ. ID. NO. 38 G A C C A A A A C A A A C C G T A T C C A C C G A
SEQ. ID. NO. 34 T G C C C A G C G G C C A C G C T T C A T C A G T
SEQ. ID. NO. 30 C T T C A T T G C C A A G C C A T C C A C G G C A
SEQ. ID. NO. 26 T G C C C A G C G G C C A C G C T T C A T C A G T

SEQ. ID. NO. 38 A T A T T T G A G C A G G G G A A G A A A T C T G
SEQ. ID. NO. 34 C C T G C C T C A C A G G T G G C C A T C T G C C
SEQ. ID. NO. 30 G T G T G T A C C T T A C G G C G T C T T G G T T
SEQ. ID. NO. 26 C C T G C C T C A C A G G T G G C C A T C T G C C

SEQ. ID. NO. 38 T C A C A G C G C C C A A G T T C A T T A G T C C
SEQ. ID. NO. 34 T G G C A C T T A T C T C G G G C C A G C T G C T
SEQ. ID. NO. 30 T G G G C A C T G C C T T C T C T G T C T G C T A
SEQ. ID. NO. 26 T G G C A C T T A T C T C G G G C C A G C T G C T

SEQ. ID. NO. 38 A G C A T C T C A G C T G G T G A T C A C C T T C
SEQ. ID. NO. 34 C A T C G T G G T C G C C T G G C T G G T G G T G
SEQ. ID. NO. 30 C T C A G C C C T G C T C A C C A A G A C C A A C
SEQ. ID. NO. 26 C A T C G T G G T C G C C T G G C T G G T G G T G

SEQ. ID. NO. 38 A G C C T C A T C T C C G T C C A G C T C C T T G
SEQ. ID. NO. 34 G A G G C A C C G G G C A C A G G C A A G G A G A
SEQ. ID. NO. 30 C G C A T T G C A C G C A T C T T C G G T G G G G
SEQ. ID. NO. 26 G A G G C A C C G G G C A C A G G C A A G G A G A

SEQ. ID. NO. 38 G A G T G T T T G T C T G G T T T G T T G T G G A
SEQ. ID. NO. 34 C A G C C C C C G A A C G G C G G G A G G T G G T
SEQ. ID. NO. 30 C C C G G G A G G G T G C C C A G C G G C C A C G
SEQ. ID. NO. 26 C A G C C C C C G A A C G G C G G G A G G T G G T

SEQ. ID. NO. 38 T C C C C C C C A C A T C A T C A T T G A C T A T
SEQ. ID. NO. 34 G A C A C T G C G C T G C A A C C A C C G C G A T
SEQ. ID. NO. 30 C T T C A T C A G T C C T G C C T C A C A G G T G
SEQ. ID. NO. 26 G A C A C T G C G C T G C A A C C A C C G C G A T

SEQ. ID. NO. 38 G G A G A G C A G C G G A C A C T A G A T C C A G
SEQ. ID. NO. 34 G C A A G T A T G T T G G G C T C G C T G G C C T
SEQ. ID. NO. 30 G C C A T C T G C C T G G C A C T T A T C T C G G
SEQ. ID. NO. 26 G C A A G T A T G T T G G G C T C G C T G G C C T

FIG. 9k.

SUBSTITUTE SHEET (RULE 26)

52/III

SEQ. ID. NO. 38 A G A A G G C C A G G G G A G T G C T C A A G T G
SEQ. ID. NO. 34 A C A A T G T G C T C C T C A T C G C G C T C T G
SEQ. ID. NO. 30 G C C A G C T G C T C A T C G T G G T C G C C T G
SEQ. ID. NO. 26 A C A A T G T G C T C C T C A T C G C G C T C T G

SEQ. ID. NO. 38 T G A C A T T T C T G A T C T C T C A C T C A T T
SEQ. ID. NO. 34 C A C G C T T T A T G C C T T C A A G A C T C G C
SEQ. ID. NO. 30 G C T G G T G G T G G A G G C A C C G G G C A C A
SEQ. ID. NO. 26 C A C G C T T T A T G C C T T C A A T A C T C G C

SEQ. ID. NO. 38 T G T T C A C T T G G A T A C A G T A T C C T C T
SEQ. ID. NO. 34 A A G T G C C C C G A A A A C T T T C A A C G A G G
SEQ. ID. NO. 30 G G C A A G G A G A C A G C C C C C G A A C G G C
SEQ. ID. NO. 26 A A G T G C C C C G A A A A C T T C A A C G A G G

SEQ. ID. NO. 38 T G A T G G T C A C T T G T A C T G T T T A T G C
SEQ. ID. NO. 34 C C A A G T T C A T T G G C T T C A C C A T G T A
SEQ. ID. NO. 30 G G G A G G T G G T G A C A C T G C G C T G C A A
SEQ. ID. NO. 26 C C A A G T T C A T T G G C T T C A C C A T G T A

SEQ. ID. NO. 38 C A T T A A A A C G A G A G G T G T C C C A G A G
SEQ. ID. NO. 34 C A C C A C C T G C A T C A T C T G G C T G G C A
SEQ. ID. NO. 30 C C A C C G C G A T G C A A G T A T G T T G G G C
SEQ. ID. NO. 26 C A C C A C C T G C A T C A T C T G G C T G G C A

SEQ. ID. NO. 38 A C T T T C A A T G A A G C C A A A C C T A T T G
SEQ. ID. NO. 34 T T C C T G C C C A T C T T C T A T G T C A C C T
SEQ. ID. NO. 30 T C G C T G G C C T A C A A T G T G C T C C T C A
SEQ. ID. NO. 26 T T G T T G C C C A T C T T C T A T G T C A C C T

SEQ. ID. NO. 38 G A T T T A C C A T G T A T A C C A C C T G C A T
SEQ. ID. NO. 34 C C A G T G A C T A C C G G G T A C A G A C C A C
SEQ. ID. NO. 30 T C G C G C T C T G C A C G C T T T A T G C C T T
SEQ. ID. NO. 26 C C A G T G A C T A C C G G G T A C A G A C C A C

SEQ. ID. NO. 38 C A T T T G G T T A G C T T T C A T C C C C A T C
SEQ. ID. NO. 34 C A C C A T G T G C G T G T C A G T C A G C C T C
SEQ. ID. NO. 30 C A A T A C T C G C A A G T G C C C C G A A A A C
SEQ. ID. NO. 26 C A C C A T G T G C G T G T C A G T C A G C C T C

FIG. 9L.

SUBSTITUTE SHEET (RULE 26)

53/III

SEQ. ID. NO. 38 T T T T T T G G T A C A G C C C A G T C A G C A G
SEQ. ID. NO. 34 A G C G G C T C C G T G G T G C T T G G C T G C C
SEQ. ID. NO. 30 T T C A A C G A G G C C A A G T T C A T T G G C T
SEQ. ID. NO. 26 A G C G G C T C C G T G G T G C T T G G C T G C C

SEQ. ID. NO. 38 A A A A G A T G T A C A T C C A G A C A A C A A C
SEQ. ID. NO. 34 T C T T T G C G C C C A A G C T G C A C A T C A T
SEQ. ID. NO. 30 T C A C C A T G T A C A C C A C C T G C A T C A T
SEQ. ID. NO. 26 T C T T T G C G C C C A A G C T G C A C A T C A T

SEQ. ID. NO. 38 A C T T A C T G T C T C C A T G A G T T T A A G T
SEQ. ID. NO. 34 C C T C T T C C A G C C G C A G A A G A A C A C C
SEQ. ID. NO. 30 C T G G C T G G C A T T G T T G C C C A T C T T C
SEQ. ID. NO. 26 C C T C T T C C A G C C G C A G A A G A A C G T G

SEQ. ID. NO. 38 G C T T C A G T A T C T C T G G G C A T G C T C T
SEQ. ID. NO. 34 A T C G A G G A G G T G C G T T G C A G C A C C G
SEQ. ID. NO. 30 T A T G T C A C C T C C A G T G A C T A C C G G G
SEQ. ID. NO. 26 G T T A G C C A C C G G G C A C C C A C C A G C C

SEQ. ID. NO. 38 A T A T G C C C A A G G T T T A T A T T A T A A T
SEQ. ID. NO. 34 C A G C T C A C G C T T T C A A G G T G G C T G C
SEQ. ID. NO. 30 T A C A G A C C A C C A C C A T G T G C G T G T C
SEQ. ID. NO. 26 G C T T T G G C A G T G C T G C T G C C A G G G C

SEQ. ID. NO. 38 T T T T C A T C C A G A A C A G A A T A C C A T C
SEQ. ID. NO. 34 C C G G G C C A C G C T G C G C C G C A G C A A C
SEQ. ID. NO. 30 A G T C A G C C T C A G C G G C T C C G T G G T G
SEQ. ID. NO. 26 C A G C T C C A G C C T T G G C C A A G G G T C T

SEQ. ID. NO. 38 G A G G A G G T G C G T T G C A G C A C C G C A G
SEQ. ID. NO. 34 G T C T C C C G C A A G C G G G T C C A G C A G C C
SEQ. ID. NO. 30 C T T G G C T G C C T C T T T G C G C C C A A G C
SEQ. ID. NO. 26 G G C T C C C A G T T T G T C C C C A C T G T T T

SEQ. ID. NO. 38 C T C A C G C T T T C A A G G T G G C T G C C C G
SEQ. ID. NO. 34 T T G G A G G C T C C A C G G G A T C C A C C C C
SEQ. ID. NO. 30 T G C A C A T C A T C C T C T T C C A G C C G C A
SEQ. ID. NO. 26 G C A A T G G C C G T G A G G T G G T G G A C T C

FIG. 9m.

54/III

SEQ. ID. NO. 38 G G C C A C G C T G C G C C G C A G C A A C G T C
SEQ. ID. NO. 34 C T C C T C C T C C A T C A G C A G C A A G A G C
SEQ. ID. NO. 30 G A A G A A C G T G G T T A G C C A C C G G G C A
SEQ. ID. NO. 26 G A C A A C G T C A T C G C T T

SEQ. ID. NO. 38 T C C C G C A A G C G G T C C A G C A G C C T T G
SEQ. ID. NO. 34 A A C A G C G A A G A C C C A T T C C C A C A G C
SEQ. ID. NO. 30 C C C A C C A G C C G C T T T G G C A G T G C T G
SEQ. ID. NO. 26

SEQ. ID. NO. 38 G A G G C T C C A C G G G A T C C A C C C C C T C
SEQ. ID. NO. 34 C C G A G A G G C A G A A G C A G C A G C A G C C
SEQ. ID. NO. 30 C T G C C A G G G C C A G C T C C A G C C T T G G
SEQ. ID. NO. 26

SEQ. ID. NO. 38 C T C C T C C A T C A G C A G C A A G A G C A A C
SEQ. ID. NO. 34 G C T G G C C C T A A C C C A G C A A G A G C A G
SEQ. ID. NO. 30 C C A A G G G T C T G G C T C C C A G T T T G T C
SEQ. ID. NO. 26

SEQ. ID. NO. 38 A G C G A A G A C C C A T T C C C A C A G C C C G
SEQ. ID. NO. 34 C A G C A G C A G C C C C T G A C C C T C C C A C
SEQ. ID. NO. 30 C C C A C T G T T T G C A A T G G C C G T G A G G
SEQ. ID. NO. 26

SEQ. ID. NO. 38 A G A G G C A G A A G C A G C A G C A G C C G C T
SEQ. ID. NO. 34 A G C A G C A A C G A T C T C A G C A G C A G C C
SEQ. ID. NO. 30 T G G T G G A C T C G A C A A C G T C A T C G C T
SEQ. ID. NO. 26

SEQ. ID. NO. 38 G G C C C T A A C C C A G C A A G A G C A G C A G
SEQ. ID. NO. 34 C A G A T G C A A G C A G A A G G T C A T C T T T
SEQ. ID. NO. 30 T
SEQ. ID. NO. 26

SEQ. ID. NO. 38 C A G C A G C C C C T G A C C C T C C C A C A G C
SEQ. ID. NO. 34 G G C A G C G G C A C G G T C A C C T T C T C A C
SEQ. ID. NO. 30
SEQ. ID. NO. 26

FIG. 9n.

55/III

SEQ. ID. NO. 38 A G C A A C G A T C T C A G C A G C A G C C C A G
SEQ. ID. NO. 34 T G A G C T T T G A T G A G C C T C A G A A G A A
SEQ. ID. NO. 30
SEQ. ID. NO. 26

SEQ. ID. NO. 38 A T G C A A G C A G A A G G T C A T C T T T G G C
SEQ. ID. NO. 34 C G C C A T G G C C C A C G G G A A T T C T A C G
SEQ. ID. NO. 30
SEQ. ID. NO. 26

SEQ. ID. NO. 38 A G C G G C A C G G T C A C C T T C T C A C T G A
SEQ. ID. NO. 34 C A C C A G A A C T C C C T G G A G G C C C A G A
SEQ. ID. NO. 30
SEQ. ID. NO. 26

SEQ. ID. NO. 38 G C T T T G A T G A G C C T C A G A A G A A C G C
SEQ. ID. NO. 34 A A A G C A G C G A T A C G C T G A C C C G A C A
SEQ. ID. NO. 30
SEQ. ID. NO. 26

SEQ. ID. NO. 38 C A T G G C C C A C G G G A A T T C T A C G C A C
SEQ. ID. NO. 34 C C A G C C A T T A C T C C C G C T G C A G T G C
SEQ. ID. NO. 30
SEQ. ID. NO. 26

SEQ. ID. NO. 38 C A G A A C T C C C T G G A G G C C C A G A A A A
SEQ. ID. NO. 34 G G G G A A A C G G A C T T A G A T C T G A C C G
SEQ. ID. NO. 30
SEQ. ID. NO. 26

SEQ. ID. NO. 38 G C A G C G A T A C G C T G A C C C G A C A C C A
SEQ. ID. NO. 34 T C C A G G A A A C A G G T C T G C A A G G A C C
SEQ. ID. NO. 30
SEQ. ID. NO. 26

SEQ. ID. NO. 38 G C C A T T A C T C C C G C T G C A G T G C G G G
SEQ. ID. NO. 34 T G T G G G T G G A G A C C A G C G G C C A G A G
SEQ. ID. NO. 30
SEQ. ID. NO. 26

FIG. 90.

SUBSTITUTE SHEET (RULE 26)

56/III

SEQ. ID. NO. 38 G A A A C G G A C T T A G A T C T G A C C G T C C
SEQ. ID. NO. 34 G T G G A G G A C C C T G A A G A G T T G T C C C
SEQ. ID. NO. 30
SEQ. ID. NO. 26

SEQ. ID. NO. 38 A G G A A A C A G G T C T G C A A G G A C C T G T
SEQ. ID. NO. 34 C A G C A C T T G T A G T G T C C A G T T C A C A
SEQ. ID. NO. 30
SEQ. ID. NO. 26

SEQ. ID. NO. 38 G G G T G G A G A C C A G C G G C C A G A G G T G
SEQ. ID. NO. 34 G A G C T T T G T C A T C A G T G G T G G A G G C
SEQ. ID. NO. 30
SEQ. ID. NO. 26

SEQ. ID. NO. 38 G A G G A C C C T G A A G A G T T G T C C C C A G
SEQ. ID. NO. 34 A G C A C T G T T A C A G A A A A C G T A G T G A
SEQ. ID. NO. 30
SEQ. ID. NO. 26

SEQ. ID. NO. 38 C A C T T G T A G T G T C C A G T T C A C A G A G
SEQ. ID. NO. 34 A T T C A
SEQ. ID. NO. 30
SEQ. ID. NO. 26

SEQ. ID. NO. 38 C T T T G T C A T C A G T G G T G G A G G C A G C
SEQ. ID. NO. 34
SEQ. ID. NO. 30
SEQ. ID. NO. 26

SEQ. ID. NO. 38 A C T G T T A C A G A A A A C G T A G T G A A T T
SEQ. ID. NO. 34
SEQ. ID. NO. 30
SEQ. ID. NO. 26

SEQ. ID. NO. 38 C A
SEQ. ID. NO. 34
SEQ. ID. NO. 30
SEQ. ID. NO. 26

FIG. 9p.

SUBSTITUTE SHEET (RULE 26)

57/III

ClustalW Formatted Alignments

SEQ. ID. NO. 39 M V C E G K R S A S C P C F F L L T A K F Y W I L
 SEQ. ID. NO. 35 M G S L L A L P A L L L L W G A V A E G P A K K V
 SEQ. ID. NO. 31 M A F Y S C C W V L L A L T W H T S A Y G P D Q R
 SEQ. ID. NO. 27 M G S L L A L L A L L P L W G A V A E G P A K K V

SEQ. ID. NO. 39 T M M Q R T H S Q E Y A H S I R V D G D I I L G G
 SEQ. ID. NO. 35 L T L E G D L V L G G L F P V H Q K G G P A E D C
 SEQ. ID. NO. 31 A Q K K G D I I L G G L F P I H F G V A A K D Q D
 SEQ. ID. NO. 27 L T L E G D L V L G G L F P V H Q K G G P A E D C

SEQ. ID. NO. 39 L F P V H A K G E R G V P C G E L K K E K G I H R
 SEQ. ID. NO. 35 G P V N E H R G I Q R L E A M L F A L D R I N R D
 SEQ. ID. NO. 31 L K S R P E S V E C I R Y N F R G F R W L Q A M I
 SEQ. ID. NO. 27 G P V N E H R G I Q R L E A M L F A L D R I N R D

SEQ. ID. NO. 39 L E A M L Y A I D Q I N K D P D L L S N I T L G V
 SEQ. ID. NO. 35 P H L L P G V R L G A H I L D S C S K D T H A L E
 SEQ. ID. NO. 31 F A I E E I N S S P A L L P N L T L G Y R I F D T
 SEQ. ID. NO. 27 P H L L P G V R L G A H I L D S C S K D T H A L E

SEQ. ID. NO. 39 R I L D T C S R D T Y A L E Q S L T F V Q A L I E
 SEQ. ID. NO. 35 Q A L D F V R A S L S R G A D G S R H I C P D G S
 SEQ. ID. NO. 31 C N T V S K A L E A T L S F V A Q N K I D S L N L
 SEQ. ID. NO. 27 Q A L D F V R A S L S R G A D G S R H I C P D G S

SEQ. ID. NO. 39 K D A S D V K C A N G D P P I F T K P D K I S G V
 SEQ. ID. NO. 35 Y A T H G D A P T A I T G V I G G S Y S D V S I Q
 SEQ. ID. NO. 31 D E F C N C S E H I P S T I A V V G A T G S G V S
 SEQ. ID. NO. 27 Y A T H G D A P T A I T G V I G G S Y S D V S I Q

SEQ. ID. NO. 39 I G A A A S S V S I M V A N I L R L F K I P Q I S
 SEQ. ID. NO. 35 V A N L L R L F Q I P Q I S Y A S T S A K L S D K
 SEQ. ID. NO. 31 T A V A N L L G L F Y I P Q V S Y A S S S R L L S
 SEQ. ID. NO. 27 V A N L L R L F Q I P Q I S Y A S T S A K L S D K

SEQ. ID. NO. 39 Y A S T A P E L S D N T R Y D F F S R V V P P D S
 SEQ. ID. NO. 35 S R Y D Y F A R T V P P D F F Q A K A M A E I L R
 SEQ. ID. NO. 31 N K N Q F K S F L R T I P N D E H Q A T A M A D I
 SEQ. ID. NO. 27 S R Y D Y F A R T V P P D F F Q A K A M A E I L R

FIG. 10a.

SUBSTITUTE SHEET (RULE 26)

58/III

SEQ. ID. NO. 39 YQAQAMVDIVTALGWNYVSTLASEG
SEQ. ID. NO. 35 FFNWTYVSTVASSEGDYGETGIEAFE
SEQ. ID. NO. 31 IEYFRWNWVGTTAADDYGRPGIEK
SEQ. ID. NO. 27 FFNWTYVSTEASSEGDYGETGIEAFE

SEQ. ID. NO. 39 NYGESGV E AFTQISREIGGVCI AQ S
SEQ. ID. NO. 35 LEARARNICVATSEKVGGRAMSRAAF
SEQ. ID. NO. 31 FREEAEERDIDFSELISQYSDEE
SEQ. ID. NO. 27 LEARARNICVATSEKVGGRAMSRAAF

SEQ. ID. NO. 39 QKIPREPRPGEFEKIIKRLLLETPNA
SEQ. ID. NO. 35 EGVVRALLQKPSARVAVLFTTRSEDA
SEQ. ID. NO. 31 EIQHVVEVIQNSTAKVIVVFSSGPD
SEQ. ID. NO. 27 EGVVRALLQKPSARVAVLFTTRSEDA

SEQ. ID. NO. 39 RAVIMFANEDDIRRILEAAKKLNQS
SEQ. ID. NO. 35 REL LAASQRLNASFTWVASD GWGAL
SEQ. ID. NO. 31 LEPLIKEIVRRNITGKIWLASEAWA
SEQ. ID. NO. 27 REL LAASQRLNASFTWVASD GWGAL

SEQ. ID. NO. 39 GHFLWIGSDSWGSKIAPVYQQEEIA
SEQ. ID. NO. 35 ESVVAGSEGA AEGAITIELASYPIS
SEQ. ID. NO. 31 SSSLIAM PQYFHVVG GTIGFALKAG
SEQ. ID. NO. 27 ESVVAGSEGA AEGAITIELASYPIS

SEQ. ID. NO. 39 EGAVTILPKRASIDGFDRYFRSRTL
SEQ. ID. NO. 35 DFASYFQSLDPWNN SRNPWFREFWE
SEQ. ID. NO. 31 QIPGFRFLKKVHPRKSVHNGFAKE
SEQ. ID. NO. 27 DFASYFQSLDPWNN SRNPWFREFWE

SEQ. ID. NO. 39 ANNRRNVWF AEFWEENFGCKLGSHG
SEQ. ID. NO. 35 QRFRC SFRQRDCAAHSLRAVPFEQE
SEQ. ID. NO. 31 FWEETFNCHLQEGAKGPLPVDTF LR
SEQ. ID. NO. 27 QRFRC SFRQRDCAAHSLRAVPFEQE

SEQ. ID. NO. 39 KRNSHIKKCTGLERIARDSSYEQEG
SEQ. ID. NO. 35 SKIMFVVNAVYAMAHALHNMHRALC
SEQ. ID. NO. 31 GHEESGDRFSNSSTA FRPLCTGDEN
SEQ. ID. NO. 27 SKIMFVVNAVYAMAHALHNMHRALC

FIG. 10b.

59/III

SEQ. ID. NO. 39 K V Q F V I D A V Y S M A Y A L H N M H K D L C P
 SEQ. ID. NO. 35 P N T T R L C D A M R P V N G R R L Y K D F V L N
 SEQ. ID. NO. 31 I S S V E T P Y I D Y T H L R I S Y N V Y L A V Y
 SEQ. ID. NO. 27 P N T T R L C D A M R P V N G R R L Y K D F V L N

SEQ. ID. NO. 39 G Y I G L C P R M S T I D G K E L L G Y I R A V N
 SEQ. ID. NO. 35 V K F D A P F R P A D T H N E V R F D R F G D G I
 SEQ. ID. NO. 31 S I A H A L Q D I Y T C L P G R G L F T N G S C A
 SEQ. ID. NO. 27 V K F D A P F R P A D T H N E V R F D R F G D G I

SEQ. ID. NO. 39 F N G S A G T P V T F N E N G D A P G R Y D I F Q
 SEQ. ID. NO. 35 G R Y N I F T Y L R A G S G R Y R Y Q K V G Y W A
 SEQ. ID. NO. 31 D I K K V E A W Q V L K H L R H L N F T N N M G E
 SEQ. ID. NO. 27 G R Y N I F T Y L R A G S G R Y R Y Q K V G Y W A

SEQ. ID. NO. 39 Y Q I T N K S T E Y K V I G H W T N Q L H L K V E
 SEQ. ID. NO. 35 E G L T L D T S L I P W A S P S A G P L P A S R C
 SEQ. ID. NO. 31 Q V T F D E C G D L V G N Y S I I N W H L S P E D
 SEQ. ID. NO. 27 E G L T L D T S L I P W A S P S A G P L A A S R C

SEQ. ID. NO. 39 D M Q W A H R E H T H P A S V C S L P C K P G E R
 SEQ. ID. NO. 35 S E P C L Q N E V K S V Q P G E V C C W L C I P C
 SEQ. ID. NO. 31 G S I V F K E V G Y Y N V Y A K K G E R L F I N E
 SEQ. ID. NO. 27 S E P C L Q N E V K S V Q P G E V C C W L C I P C

SEQ. ID. NO. 39 K K T V K G V P C C W H C E R C E G Y N Y Q V D E
 SEQ. ID. NO. 35 Q P Y E Y R L D E F T C A D C G L G Y W P N A S L
 SEQ. ID. NO. 31 E K I L W S G F S R E V P F S N C S R D C L A G T
 SEQ. ID. NO. 27 Q P Y E Y R L D E F T C A D C G L G Y W P N A S L

SEQ. ID. NO. 39 L S C E L C P L D Q R P N M N R T G C Q L I P I I
 SEQ. ID. NO. 35 T G C F E L P Q E Y I R W G D A W A V G P V T I A
 SEQ. ID. NO. 31 R K G I I E G E P T C C F E C V E C P D G E Y S D
 SEQ. ID. NO. 27 T G C F E L P Q E Y I R W G D A W A V G P V T I A

SEQ. ID. NO. 39 K L E W H S P W A V V P V F V A I L G I I A T T F
 SEQ. ID. NO. 35 C L G A L A T L F V L G V F V R H N A T P V V K A
 SEQ. ID. NO. 31 E T D A S A C N K C P D D F W S N E N H T S C F E
 SEQ. ID. NO. 27 C L G A L A T L F V L G V F V R H N A T P V V K A

FIG. 10c.

60/III

SEQ. ID. NO. 39 V I V T F V R Y N D T P I V R A S G R E L S Y V L
 SEQ. ID. NO. 35 S G R E L C Y I L L G G V F L C Y C M T F I F I A
 SEQ. ID. NO. 31 L P Q E Y I R W G D A W A V G P V T I A C L G A L
 SEQ. ID. NO. 27 S G R E L C Y I L L G G V F L C Y C M T F I F I A

SEQ. ID. NO. 39 L T G I F L C Y S I T F L M I A A P D T I I C S F
 SEQ. ID. NO. 35 K P S T A V C T L R R L G L G T A F S V C Y S A L
 SEQ. ID. NO. 31 A T L F V L G V F V R H N A T P V V K A S G R E L
 SEQ. ID. NO. 27 K P S T A V C T L R R L G L G T A F S V C Y S A L

SEQ. ID. NO. 39 R R V F L G L G M C F S Y A A L L T K T N R I H R
 SEQ. ID. NO. 35 L T K T N R I A R I F G G A R E G A Q R P R F I S
 SEQ. ID. NO. 31 C Y I L L G G V F L C Y C M T F I F I A K P S T A
 SEQ. ID. NO. 27 L T K T N R I A R I F G G A R E G A Q R P R F I S

SEQ. ID. NO. 39 I F E Q G K K S V T A P K F I S P A S Q L V I T F
 SEQ. ID. NO. 35 P A S Q V A I C L A L I S G Q L L I V V A W L V V
 SEQ. ID. NO. 31 V C T L R R L G L G T A F S V C Y S A L L T K T N
 SEQ. ID. NO. 27 P A S Q V A I C L A L I S G Q L L I V V A W L V V

SEQ. ID. NO. 39 S L I S V Q L L G V F V W F V V D P P H I I I D Y
 SEQ. ID. NO. 35 E A P G T G K E T A P E R R E V V T L R C N H R D
 SEQ. ID. NO. 31 R I A R I F G G A R E G A Q R P R F I S P A S Q V
 SEQ. ID. NO. 27 E A P G T G K E T A P E R R E V V T L R C N H R D

SEQ. ID. NO. 39 G E Q R T L D P E K A R G V L K C D I S D L S L I
 SEQ. ID. NO. 35 A S M L G S L A Y N V L L I A L C T L Y A F K T R
 SEQ. ID. NO. 31 A I C L A L I S G Q L L I V V A W L V V E A P G T
 SEQ. ID. NO. 27 A S M L G S L A Y N V L L I A L C T L Y A F N T R

SEQ. ID. NO. 39 C S L G Y S I L L M V T C T V Y A I K T R G V P E
 SEQ. ID. NO. 35 K C P E N F N E A K F I G F T M Y T T C I I W L A
 SEQ. ID. NO. 31 G K E T A P E R R E V V T L R C N H R D A S M L G
 SEQ. ID. NO. 27 K C P E N F N E A K F I G F T M Y T T C I I W L A

SEQ. ID. NO. 39 T F N E A K P I G F T M Y T T C I I W L A F I P I
 SEQ. ID. NO. 35 F L P I F Y V T S S D Y R V Q T T T M C V S V S L
 SEQ. ID. NO. 31 S L A Y N V L L I A L C T L Y A F N T R K C P E N
 SEQ. ID. NO. 27 L L P I F Y V T S S D Y R V Q T T T M C V S V S L

FIG. 10d.

61/III

SEQ. ID. NO. 39 F F G T A Q S A E K M Y I Q T T T L T V S M S L S
SEQ. ID. NO. 35 S G S V V L G C L F A P K L H I I L F Q P Q K N T
SEQ. ID. NO. 31 F N E A K F I G F T M Y T T C I I W L A L L P I F
SEQ. ID. NO. 27 S G S V V L G C L F A P K L H I I L F Q P Q K N

SEQ. ID. NO. 39 A S V S L G M L Y M P K V Y I I I F H P E Q N T I
SEQ. ID. NO. 35 I E E V R C S T A A H A F K V A A R A T L R R S N
SEQ. ID. NO. 31 Y V T S S D Y R V Q T T T M C V S V S L S G S V V
SEQ. ID. NO. 27

SEQ. ID. NO. 39 E E V R C S T A A H A F K V A A R A T L R R S N V
SEQ. ID. NO. 35 V S R K R S S S L G G S T G S T P S S S I S S K S
SEQ. ID. NO. 31 L G C L F A P K L H I I L F Q P Q K N V V S H R A
SEQ. ID. NO. 27

SEQ. ID. NO. 39 S R K R S S S L G G S T G S T P S S S I S S K S N
SEQ. ID. NO. 35 N S E D P F P Q P E R Q K Q Q Q P L A L T Q Q E Q
SEQ. ID. NO. 31 P T S R F G S A A A R A S S S L G Q G S G S Q F V
SEQ. ID. NO. 27

SEQ. ID. NO. 39 S E D P F P Q P E R Q K Q Q Q P L A L T Q Q E Q Q
SEQ. ID. NO. 35 Q Q Q P L T L P Q Q Q R S Q Q Q P R C K Q K V I F
SEQ. ID. NO. 31 P T V C N G R E V V D S T T S S L
SEQ. ID. NO. 27

SEQ. ID. NO. 39 Q Q P L T L P Q Q Q R S Q Q Q P R C K Q K V I F G
SEQ. ID. NO. 35 G S G T V T F S L S F D E P Q K N A M A H G N S T
SEQ. ID. NO. 31
SEQ. ID. NO. 27

SEQ. ID. NO. 39 S G T V T F S L S F D E P Q K N A M A H G N S T H
SEQ. ID. NO. 35 H Q N S L E A Q K S S D T L T R H Q P L L P L Q C
SEQ. ID. NO. 31
SEQ. ID. NO. 27

SEQ. ID. NO. 39 Q N S L E A Q K S S D T L T R H Q P L L P L Q C G
SEQ. ID. NO. 35 G E T D L D L T V Q E T G L Q G P V G G D Q R P E
SEQ. ID. NO. 31
SEQ. ID. NO. 27

FIG. 10e.

62/III

SEQ. ID. NO. 39 E T D L D L T V Q E T G L Q G P V G G D Q R P E V
SEQ. ID. NO. 35 V E D P E E L S P A L V V S S S Q S F V I S G G G
SEQ. ID. NO. 31
SEQ. ID. NO. 27

SEQ. ID. NO. 39 E D P E E L S P A L V V S S S Q S F V I S G G G S
SEQ. ID. NO. 35 S T V T E N V V N S
SEQ. ID. NO. 31
SEQ. ID. NO. 27

SEQ. ID. NO. 39 T V T E N V V N S
SEQ. ID. NO. 35
SEQ. ID. NO. 31
SEQ. ID. NO. 27

FIG. 10f.

63/III

ClustalW Formatted Alignments

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SEQ. ID. NO. 40 A T G G T A T G C G A G G G A A A G C G A T C A G
SEQ. ID. NO. 46 A T G G G A T C G C T G C T T G C G C T C C C G G
SEQ. ID. NO. 36 A T G G G A T C G C T G C T T G C G C T C C C G G
SEQ. ID. NO. 32 A T G G C A T T T T A T A G C T G C T G C T G G G

SEQ. ID. NO. 40 C C T C T T G C C C T T G T T T C T T C C T C T T
SEQ. ID. NO. 46 C A C T G C T G C T G C T G T G G G G T G C T G T
SEQ. ID. NO. 36 C A C T G C T G C T G C T G T G G G G T G C T G T
SEQ. ID. NO. 32 T C C T C T T G G C A C T C A C C T G G C A C A C

SEQ. ID. NO. 40 G A C C G C C A A G T T C T A C T G G A T C C T C
SEQ. ID. NO. 46 G G C T G A G G G C C C A G C C A A G A A G G T G
SEQ. ID. NO. 36 G G C T G A G G G C C C A G C C A A G A A G G T G
SEQ. ID. NO. 32 C T C T G C C T A C G G G C C A G A C C A G C G A

SEQ. ID. NO. 40 A C A A T G A T G C A A A G A A C T C A C A G C C
SEQ. ID. NO. 46 C T G A C C C T G G A G G G A G A C T T G G T G C
SEQ. ID. NO. 36 C T G A C C C T G G A G G G A G A C T T G G T G C
SEQ. ID. NO. 32 G C C C A A A A G A A A G G G G G A C A T T A T C C

SEQ. ID. NO. 40 A G G A G T A T G C C C A T T C C A T A C G G G T
SEQ. ID. NO. 46 T G G G T G G G C T G T T C C C A G T G C A C C A
SEQ. ID. NO. 36 T G G G T G G G C T G T T C C C A G T G C A C C A
SEQ. ID. NO. 32 T T G G G G G G C T C T T T C C T A T T C A T T T

SEQ. ID. NO. 40 G G A T G G G G A C A T T A T T T T G G G G G G T
SEQ. ID. NO. 46 G A A G G G C G G C C C A G C A G A G G A C T G T
SEQ. ID. NO. 36 G A A G G G C G G C C C A G C A G A G G A C T G T
SEQ. ID. NO. 32 T G G A G T A G C A G C T A A A G A T C A A G A T

SEQ. ID. NO. 40 C T C T T C C C T G T C C A C G C A A A G G G A G
SEQ. ID. NO. 46 G G T C C T G T C A A T G A G C A C C G T G G C A
SEQ. ID. NO. 36 G G T C C T G T C A A T G A G C A C C G T G G C A
SEQ. ID. NO. 32 C T C A A A T C A A G G C C G G A G T C T G T G G

SEQ. ID. NO. 40 A G A G A G G G G T G C C T T G T G G G G A G C T
SEQ. ID. NO. 46 T C C A G C G C C T G G A G G C C A T G C T T T T
SEQ. ID. NO. 36 T C C A G C G C C T G G A G G C C A T G C T T T T
SEQ. ID. NO. 32 A A T G T A T C A G G T A T A A T T T C C G T G G
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FIG. 11a.

64/III

SEQ. ID. NO. 40 G A A G A A G G A A A G G G G A T T C A C A G A
SEQ. ID. NO. 46 T G C A C T G G A C C G C A T C A A C C G T G A C
SEQ. ID. NO. 36 T G C A C T G G A C C G C A T C A A C C G T G A C
SEQ. ID. NO. 32 G T T T C G C T G G T T A C A G G C T A T G A T A

SEQ. ID. NO. 40 C T G G A G G C C A T G C T T T A T G C A A T T G
SEQ. ID. NO. 46 C C G C A C C T G C T G C C T G G C G T G C G C C
SEQ. ID. NO. 36 C C G C A C C T G C T G C C T G G C G T G C G C C
SEQ. ID. NO. 32 T T T G C C A T A G A G G A G A T A A A C A G C A

SEQ. ID. NO. 40 A C C A G A T T A A C A A G G A C C C T G A T C T
SEQ. ID. NO. 46 T G G G T G C A C A C A T C C T C G A C A G T T G
SEQ. ID. NO. 36 T G G G T G C A C A C A T C C T C G A C A G T T G
SEQ. ID. NO. 32 G C C C A G C C C T T C T T C C C A A C T T G A C

SEQ. ID. NO. 40 C C T T T C C A A C A T C A C T C T G G G T G T C
SEQ. ID. NO. 46 C T C C A A G G A C A C A C A T G C G C T G G A G
SEQ. ID. NO. 36 C T C C A A G G A C A C A C A T G C G C T G G A G
SEQ. ID. NO. 32 G C T G G G A T A C A G G A T A T T T G A C A C T

SEQ. ID. NO. 40 C G C A T C C T C G A C A C G T G C T C T A G G G
SEQ. ID. NO. 46 C A G G C A C T G G A C T T T G T G C G T G C C T
SEQ. ID. NO. 36 C A G G C A C T G G A C T T T G T G C G T G C C T
SEQ. ID. NO. 32 T G C A A C A C C G T T T C T A A G G C C T T G G

SEQ. ID. NO. 40 A C A C C T A T G C T T T G G A G C A G T C T C T
SEQ. ID. NO. 46 C A C T C A G C C G T G G T G C T G A T G G C T C
SEQ. ID. NO. 36 C A C T C A G C C G T G G T G C T G A T G G C T C
SEQ. ID. NO. 32 A A G C C A C C C T G A G T T T T G T T G C T C A

SEQ. ID. NO. 40 A A C A T T C G T G C A G G C A T T A A T A G A G
SEQ. ID. NO. 46 A C G C C A C A T C T G C C C C G A C G G C T C T
SEQ. ID. NO. 36 A C G C C A C A T C T G C C C C G A C G G C T C T
SEQ. ID. NO. 32 A A A C A A A A T T G A T T C T T T G A A C C T T

SEQ. ID. NO. 40 A A A G A T G C T T C G G A T G T G A A G T G T G
SEQ. ID. NO. 46 T A T G C G A C C C A T G G T G A T G C T C C C A
SEQ. ID. NO. 36 T A T G C G A C C C A T G G T G A T G C T C C C A
SEQ. ID. NO. 32 G A T G A G T T C T G C A A C T G C T C A G A G C

FIG. 11b.

65/III

SEQ. ID. NO. 40 C T A A T G G A G A T C C A C C C A T T T T C A C
SEQ. ID. NO. 46 C T G C C A T C A C T G G T G T T A T T G G C G G
SEQ. ID. NO. 36 C T G C C A T C A C T G G T G T T A T T G G C G G
SEQ. ID. NO. 32 A C A T T C C C T C T A C G A T T G C T G T G G T

SEQ. ID. NO. 40 C A A G C C C G A C A A G A T T T C T G G C G T C
SEQ. ID. NO. 46 T T C C T A C A G T G A T G T C T C C A T C C A G
SEQ. ID. NO. 36 T T C C T A C A G T G A T G T C T C C A T C C A G
SEQ. ID. NO. 32 G G G A G C A A C T G G C T C A G G C G T C T C C

SEQ. ID. NO. 40 A T A G G T G C T G C A G C A A G C T C C G T G T
SEQ. ID. NO. 46 G T G G C C A A C C T C T T G A G G C T A T T T C
SEQ. ID. NO. 36 G T G G C C A A C C T C T T G A G G C T A T T T C
SEQ. ID. NO. 32 A C G G C A G T G G C A A A T C T G C T G G G G C

SEQ. ID. NO. 40 C C A T C A T G G T T G C T A A C A T T T T A A G
SEQ. ID. NO. 46 A G A T C C C A C A G A T T A G C T A C G C C T C
SEQ. ID. NO. 36 A G A T C C C A C A G A T T A G C T A C G C C T C
SEQ. ID. NO. 32 T C T T C T A C A T T C C C C A G G T C A G T T A

SEQ. ID. NO. 40 A C T T T T T A A G A T A C C T C A A A T C A G C
SEQ. ID. NO. 46 T A C C A G T G C C A A G C T G A G T G A C A A G
SEQ. ID. NO. 36 T A C C A G T G C C A A G C T G A G T G A C A A G
SEQ. ID. NO. 32 T G C C T C C T C C A G C A G A C T C C T C A G C

SEQ. ID. NO. 40 T A T G C A T C C A C A G C C C C A G A G C T A A
SEQ. ID. NO. 46 T C C C G C T A T G A C T A C T T T T G C C C G C A
SEQ. ID. NO. 36 T C C C G C T A T G A C T A C T T T T G C C C G C A
SEQ. ID. NO. 32 A A C A A G A A T C A A T T C A A G T C T T T C C

SEQ. ID. NO. 40 G T G A T A A C A C C A G G T A T G A C T T T T T
SEQ. ID. NO. 46 C A G T G C C T C C T G A C T T C T T C C A A G C
SEQ. ID. NO. 36 C A G T G C C T C C T G A C T T C T T C C A A G C
SEQ. ID. NO. 32 T C C G A A C C A T C C C C A A T G A T G A G C A

SEQ. ID. NO. 40 C T C T C G A G T G G T T C C G C C T G A C T C C
SEQ. ID. NO. 46 C A A G G C C A T G G C T G A G A T T C T C C G C
SEQ. ID. NO. 36 C A A G G C C A T G G C T G A G A T T C T C C G C
SEQ. ID. NO. 32 C C A G G C C A C T G C C A T G G C A G A C A T C

FIG. 1/c.

66/III

SEQ. ID. NO. 40 T A C C A A G C C C A A G C C A T G G T G G A C A
SEQ. ID. NO. 46 T T C T T C A A C T G G A C C T A T G T G T C C A
SEQ. ID. NO. 36 T T C T T C A A C T G G A C C T A T G T G T C C A
SEQ. ID. NO. 32 A T C G A G T A T T T C C G C T G G A A C T G G G

SEQ. ID. NO. 40 T C G T G A C A G C A C T G G G A T G G A A T T A
SEQ. ID. NO. 46 C T G T G G C G T C T G A G G G C G A C T A T G G
SEQ. ID. NO. 36 C T G T G G C G T C T G A G G G C G A C T A T G G
SEQ. ID. NO. 32 T G G G C A C A A T T G C A G C T G A T G A C G A

SEQ. ID. NO. 40 T G T T T C G A C A C T G G C T T C T G A G G G G
SEQ. ID. NO. 46 C G A G A C A G G C A T T G A G G C C T T T G A G
SEQ. ID. NO. 36 C G A G A C A G G C A T T G A G G C C T T T G A G
SEQ. ID. NO. 32 C T A T G G G C G G C C G G G G A T T G A G A A A

SEQ. ID. NO. 40 A A C T A T G G T G A G A G C G G T G T G G A G G
SEQ. ID. NO. 46 C T A G A G G C T C G T G C C C G C A A C A T C T
SEQ. ID. NO. 36 C T A G A G G C T C G T G C C C G C A A C A T C T
SEQ. ID. NO. 32 T T C C G A G A G G A A G C T G A G G A A A G G G

SEQ. ID. NO. 40 C C T T C A C C C A G A T C T C G A G G G A G A T
SEQ. ID. NO. 46 G T G T G G C C A C C T C G G A G A A A G T G G G
SEQ. ID. NO. 36 G T G T G G C C A C C T C G G A G A A A G T G G G
SEQ. ID. NO. 32 A T A T C T G C A T C G A C T T C A G T G A A C T

SEQ. ID. NO. 40 T G G T G G T G T T T G C A T T G C T C A G T C A
SEQ. ID. NO. 46 C C G T G C C A T G A G C C G C G C G G C C T T T
SEQ. ID. NO. 36 C C G T G C C A T G A G C C G C G C G G C C T T T
SEQ. ID. NO. 32 C A T C T C C A G T A C T C T G A T G A G G A A

SEQ. ID. NO. 40 C A G A A A A T C C C A C G T G A A C C A A G A C
SEQ. ID. NO. 46 G A G G G T G T G G T G C G A G C C C T G C T G C
SEQ. ID. NO. 36 G A G G G T G T G G T G C G A G C C C T G C T G C
SEQ. ID. NO. 32 G A G A T C C A G C A T G T G G T A G A G G T G A

SEQ. ID. NO. 40 C T G G A G A A T T T G A A A A A A T T A T C A A
SEQ. ID. NO. 46 A G A A G C C C A G T G C C C G C G T G G C T G T
SEQ. ID. NO. 36 A G A A G C C C A G T G C C C G C G T G G C T G T
SEQ. ID. NO. 32 T T C A A A A T T C C A C G G C C A A A G T C A T

FIG. 1Id.

SUBSTITUTE SHEET (RULE 26)

67/III

SEQ. ID. NO. 40 A C G C C T G C T A G A A A C A C C T A A T G C T
SEQ. ID. NO. 46 C C T G T T C A C C C G T T C T G A G G A T G C C
SEQ. ID. NO. 36 C C T G T T C A C C C G T T C T G A G G A T G C C
SEQ. ID. NO. 32 C G T G G T T T T C T C C A G T G G C C C A G A T

SEQ. ID. NO. 40 C G A G C A G T G A T T A T G T T T G C C A A T G
SEQ. ID. NO. 46 C G G G A G C T G C T T G C T G C C A G C C A G C
SEQ. ID. NO. 36 C G G G A G C T G C T T G C T G C C A G C C A G C
SEQ. ID. NO. 32 C T T G A G C C C C T C A T C A A G G A G A T T G

SEQ. ID. NO. 40 A G G A T G A C A T C A G G A G G A T A T T G G A
SEQ. ID. NO. 46 G C C T C A A T G C C A G C T T C A C C T G G G T
SEQ. ID. NO. 36 G C C T C A A T G C C A G C T T C A C C T G G G T
SEQ. ID. NO. 32 T C C G G C G C A A T A T C A C G G G C A A G A T

SEQ. ID. NO. 40 A G C A G C A A A A A A A C T A A A C C A A A G T
SEQ. ID. NO. 46 G G C C A G T G A T G G T T G G G G G G C C C T G
SEQ. ID. NO. 36 G G C C A G T G A T G G T T G G G G G G C C C T G
SEQ. ID. NO. 32 C T G G C T G G C C A G C G A G G C C T G G G C C

SEQ. ID. NO. 40 G G G C A T T T T C T C T G G A T T G G C T C A G
SEQ. ID. NO. 46 G A G A G T G T G G T G G C A G G C A G T G A G G
SEQ. ID. NO. 36 G A G A G T G T G G T G G C A G G C A G T G A G G
SEQ. ID. NO. 32 A G C T C C T C C C T G A T C G C C A T G C C T C

SEQ. ID. NO. 40 A T A G T T G G G G A T C C A A A A T A G C A C C
SEQ. ID. NO. 46 G G G C T G C T G A G G G T G C T A T C A C C A T
SEQ. ID. NO. 36 G G G C T G C T G A G G G T G C T A T C A C C A T
SEQ. ID. NO. 32 A G T A C T T C C A C G T G G T T G G C G G C A C

SEQ. ID. NO. 40 T G T C T A T C A G C A A G A G G A G A T T G C A
SEQ. ID. NO. 46 C G A G C T G G C C T C C T A C C C C A T C A G T
SEQ. ID. NO. 36 C G A G C T G G C C T C C T A C C C C A T C A G T
SEQ. ID. NO. 32 C A T T G G A T T C G C T C T G A A G G C T G G G

SEQ. ID. NO. 40 G A A G G G G C T G T G A C A A T T T T G C C C A
SEQ. ID. NO. 46 G A C T T T G C C T C C T A C T T C C A G A G C C
SEQ. ID. NO. 36 G A C T T T G C C T C C T A C T T C C A G A G C C
SEQ. ID. NO. 32 C A G A T C C C A G G C T T C C G G G A A T T C C

FIG. 11e.

68/III

SEQ. ID. NO. 40 A A C G A G C A T C A A T T G A T G G A T T T G A
SEQ. ID. NO. 46 T G G A C C C T T G G A A C A A C A G C C G G A A
SEQ. ID. NO. 36 T G G A C C C T T G G A A C A A C A G C C G G A A
SEQ. ID. NO. 32 T G A A G A A G G T C C A T C C C A G G A A G T C

SEQ. ID. NO. 40 T C G A T A C T T T A G A A G C C G A A C T C T T
SEQ. ID. NO. 46 C C C C T G G T T C C G T G A A T T C T G G G A G
SEQ. ID. NO. 36 C C C C T G G T T C C G T G A A T T C T G G G A G
SEQ. ID. NO. 32 T G T C C A C A A T G G T T T T G C C A A G G A G

SEQ. ID. NO. 40 G C C A A T A A T C G A A G A A A T G T G T G G T
SEQ. ID. NO. 46 C A G A G G T T C C G C T G C A G C T T C C G G C
SEQ. ID. NO. 36 C A G A G G T T C C G C T G C A G C T T C C G G C
SEQ. ID. NO. 32 T T T T G G G A A G A A A C A T T T A A C T G C C

SEQ. ID. NO. 40 T T G C A G A A T T C T G G G A G G A G A A T T T
SEQ. ID. NO. 46 A G C G A G A C T G C G C A G C C C A C T C T C T
SEQ. ID. NO. 36 A G C G A G A C T G C G C A G C C C A C T C T C T
SEQ. ID. NO. 32 A C C T C C A A G A A G G T G C A A A A G G A C C

SEQ. ID. NO. 40 T G G C T G C A A G T T A G G A T C A C A T G G G
SEQ. ID. NO. 46 C C G G G C T G T G C C C T T T G A G C A G G A G
SEQ. ID. NO. 36 C C G G G C T G T G C C C T T T G A G C A G G A G
SEQ. ID. NO. 32 T T T A C C T G T G G A C A C C T T T C T G A G A

SEQ. ID. NO. 40 A A A A G G A A C A G T C A T A T A A A G A A A T
SEQ. ID. NO. 46 T C C A A G A T C A T G T T T G T G G T C A A T G
SEQ. ID. NO. 36 T C C A A G A T C A T G T T T G T G G T C A A T G
SEQ. ID. NO. 32 G G T C A C G A A G A A A G T G G C G A C A G G T

SEQ. ID. NO. 40 G C A C A G G G C T G G A G C G A A T T G C T C G
SEQ. ID. NO. 46 C A G T G T A C G C C A T G G C C C A T G C G C T
SEQ. ID. NO. 36 C A G T G T A C G C C A T G G C C C A T G C G C T
SEQ. ID. NO. 32 T T A G C A A C A G C T C G A C A G C C T T C C G

SEQ. ID. NO. 40 G G A T T C A T C T T A T G A A C A G G A A G G A
SEQ. ID. NO. 46 C C A C A A C A T G C A C C G T G C C C T C T G C
SEQ. ID. NO. 36 C C A C A A C A T G C A C C G T G C C C T C T G C
SEQ. ID. NO. 32 A C C C C T C T G T A C A G G G G A T G A G A A C

FIG. 11f.

SUBSTITUTE SHEET (RULE 26)

69/III

SEQ. ID. NO. 40 A A G G T C C A A T T T G T A A T T G A T G C T G
SEQ. ID. NO. 46 C C C A A C A C C A C C C G G C T C T G T G A C G
SEQ. ID. NO. 36 C C C A A C A C C A C C C G G C T C T G T G A C G
SEQ. ID. NO. 32 A T C A G C A G T G T C G A G A C C C C T T A C A

SEQ. ID. NO. 40 T A T A T T C C A T G G C T T A C G C C C T G C A
SEQ. ID. NO. 46 C G A T G C G G C C A G T T A A C G G G C G C C G
SEQ. ID. NO. 36 C G A T G C G G C C A G T T A A C G G G C G C C G
SEQ. ID. NO. 32 T A G A T T A C A C G C A T T T A C G G A T A T C

SEQ. ID. NO. 40 C A A T A T G C A C A A A G A T C T C T G C C C T
SEQ. ID. NO. 46 C C T C T A C A A G G A C T T T G T G C T C A A C
SEQ. ID. NO. 36 C C T C T A C A A G G A C T T T G T G C T C A A C
SEQ. ID. NO. 32 C T A C A A T G T G T A C T T A G C A G T C T A C

SEQ. ID. NO. 40 G G A T A C A T T G G C C T T T G T C C A C G A A
SEQ. ID. NO. 46 G T C A A G T T T G A T G C C C C C T T T C G C C
SEQ. ID. NO. 36 G T C A A G T T T G A T G C C C C C T T T C G C C
SEQ. ID. NO. 32 T C C A T T G C C C A C G C C T T G C A A G A T A

SEQ. ID. NO. 40 T G A G T A C C A T T G A T G G G A A A G A G C T
SEQ. ID. NO. 46 C A G C T G A C A C C C A C A A T G A G G T C C G
SEQ. ID. NO. 36 C A G C T G A C A C C C A C A A T G A G G T C C G
SEQ. ID. NO. 32 T A T A T A C C T G C T T A C C T G G G A G A G G

SEQ. ID. NO. 40 A C T T G G T T A T A T T C G G G C T G T A A A T
SEQ. ID. NO. 46 C T T T G A C C G C T T T G G T G A T G G T A T T
SEQ. ID. NO. 36 C T T T G A C C G C T T T G G T G A T G G T A T T
SEQ. ID. NO. 32 G C T C T T C A C C A A T G G C T C C T G T G C A

SEQ. ID. NO. 40 T T T A A T G G C A G T G C T G G C A C T C C T G
SEQ. ID. NO. 46 G G C C G C T A C A A C A T C T T C A C C T A T C
SEQ. ID. NO. 36 G G C C G C T A C A A C A T C T T C A C C T A T C
SEQ. ID. NO. 32 G A C A T C A A G A A A G T T G A G G C G T G G C

SEQ. ID. NO. 40 T C A C T T T T A A T G A A A A C G G A G A T G C
SEQ. ID. NO. 46 T G C G T G C A G G C A G T G G G C G C T A T C G
SEQ. ID. NO. 36 T G C G T G C A G G C A G T G G G C G C T A T C G
SEQ. ID. NO. 32 A G G T C C T G A A G C A C C T A C G G C A T C T

FIG. 11g.

SUBSTITUTE SHEET (RULE 26)

70/III

SEQ. ID. NO. 40 T C C T G G A C G T T A T G A T A T C T T C C A G
SEQ. ID. NO. 46 C T A C C A G A A G G T G G G C T A C T G G G C A
SEQ. ID. NO. 36 C T A C C A G A A G G T G G G C T A C T G G G C A
SEQ. ID. NO. 32 A A A C T T T A C A A A C A A T A T G G G G G A G

SEQ. ID. NO. 40 T A T C A A A T A A C C A A C A A A A G C A C A G
SEQ. ID. NO. 46 G A A G G C T T T G A C T C T G G A C A C C A G C C
SEQ. ID. NO. 36 G A A G G C T T T G A C T C T G G A C A C C A G C C
SEQ. ID. NO. 32 C A G G T G A C C T T T G A T G A G T G T G G T G

SEQ. ID. NO. 40 A G T A C A A A G T C A T C G G C C A C T G G A C
SEQ. ID. NO. 46 T C A T C C C A T G G G C C T C A C C C T C A G C
SEQ. ID. NO. 36 T C A T C C C A T G G G C C T C A C C C T C A G C
SEQ. ID. NO. 32 A C C T G G T G G G G A A C T A T T C C A T C A T

SEQ. ID. NO. 40 C A A T C A G C T T C A T C T A A A A G T G G A A
SEQ. ID. NO. 46 C G G C C C C C T G C C C G C C T C T C G C T G C
SEQ. ID. NO. 36 C G G C C C C C T G C C C G C C T C T C G C T G C
SEQ. ID. NO. 32 C A A C T G G C A C C T C T C C C C A G A G G A T

SEQ. ID. NO. 40 G A C A T G C A G T G G G C T C A T A G A G A A C
SEQ. ID. NO. 46 A G T G A G C C C T G C C T C C A G A A T G A G G
SEQ. ID. NO. 36 A G T G A G C C C T G C C T C C A G A A T G A G G
SEQ. ID. NO. 32 G G C T C C A T C G T G T T T A A G G A A G T C G

SEQ. ID. NO. 40 A T A C T C A C C C G G C G T C T G T C T G C A G
SEQ. ID. NO. 46 T G A A G A G T G T G C A G C C G G G C G A A G T
SEQ. ID. NO. 36 T G A A G A G T G T G C A G C C G G G C G A A G T
SEQ. ID. NO. 32 G G T A T T A C A A C G T C T A T G C C A A G A A

SEQ. ID. NO. 40 C C T G C C G T G T A A G C C A G G G G A G A G G
SEQ. ID. NO. 46 C T G C T G C T G G C T C T G C A T T C C G T G C
SEQ. ID. NO. 36 C T G C T G C T G G C T C T G C A T T C C G T G C
SEQ. ID. NO. 32 G G G A G A A A G A C T C T T C A T C A A C G A G

SEQ. ID. NO. 40 A A G A A A A C G G T G A A A G G G G T C C C T T
SEQ. ID. NO. 46 C A G C C C T A T G A G T A C C G A T T G G A C G
SEQ. ID. NO. 36 C A G C C C T A T G A G T A C C G A T T G G A C G
SEQ. ID. NO. 32 G A G A A A A T C C T G T G G A G T G G G T T C T

FIG. 11h.

SUBSTITUTE SHEET (RULE 26)

71/III

SEQ. ID. NO. 40 G C T G C T G G C A C T G T G A A C G C T G T G A
SEQ. ID. NO. 46 A A T T C A C T T G C G C T G A T T G T G G C C T
SEQ. ID. NO. 36 A A T T C A C T T G C G C T G A T T G T G G C C T
SEQ. ID. NO. 32 C C A G G G A G G T G C C C T T C T C C A A C T G

SEQ. ID. NO. 40 A G G T T A C A A C T A C C A G G T G G A T G A G
SEQ. ID. NO. 46 G G G C T A C T G G C C C A A T G C C A G C C T G
SEQ. ID. NO. 36 G G G C T A C T G G C C C A A T G C C A G C C T G
SEQ. ID. NO. 32 C A G C C G A G A C T G C C T G G C A G G G A C C

SEQ. ID. NO. 40 C T G T C C T G T G A A C T T T G C C C T C T G G
SEQ. ID. NO. 46 A C T G G C T G C T T C G A A C T G C C C C A G G
SEQ. ID. NO. 36 A C T G G C T G C T T C G A A C T G C C C C A G G
SEQ. ID. NO. 32 A G G A A A G G G A T C A T T G A G G G G G A G C

SEQ. ID. NO. 40 A T C A G A G A C C C A A C A T G A A C C G C A C
SEQ. ID. NO. 46 A G T A C A T C C G C T G G G G C G A T G C C T G
SEQ. ID. NO. 36 A G T A C A T C C G C T G G G G C G A T G C C T G
SEQ. ID. NO. 32 C C A C C T G C T G C T T T G A G T G T G T G G A

SEQ. ID. NO. 40 A G G C T G C C A G C T T A T C C C C A T C A T C
SEQ. ID. NO. 46 G G C T G T G G G A C C T G T C A C C A T C G C C
SEQ. ID. NO. 36 G G C T G T G G G A C C T G T C A C C A T C G C C
SEQ. ID. NO. 32 G T G T C C T G A T G G G G A G T A T A G T G A T

SEQ. ID. NO. 40 A A A T T G G A G T G G C A T T C T C C C T G G G
SEQ. ID. NO. 46 T G C C T C G G T G C C C T G G C C A C C C T C T
SEQ. ID. NO. 36 T G C C T C G G T G C C C T G G C C A C C C T C T
SEQ. ID. NO. 32 G A G A C A G A T G C C A G T G C C T G T A A C A

SEQ. ID. NO. 40 C T G T G G T G C C T G T G T T T G T T G C A A T
SEQ. ID. NO. 46 T T G T G C T G G G T G T C T T T G T G C G G C A
SEQ. ID. NO. 36 T T G T G C T G G G T G T C T T T G T G C G G C A
SEQ. ID. NO. 32 A G T G C C C A G A T G A C T T C T G G T C C A A

SEQ. ID. NO. 40 A T T G G G A A T C A T C G C C A C C A C C T T T
SEQ. ID. NO. 46 C A A T G C C A C A C C A G T G G T C A A G G C C
SEQ. ID. NO. 36 C A A T G C C A C A C C A G T G G T C A A G G C C
SEQ. ID. NO. 32 T G A G A A C C A C A C C T C C T G C T T C G A A

FIG. 11i

72/III

SEQ. ID. NO. 40 GTGATCGTGACCTTTGTCCGCTATA
SEQ. ID. NO. 46 TCAGGTCGGGAGCTCTGCTACATCC
SEQ. ID. NO. 36 TCAGGTCGGGAGCTCTGCTACATCC
SEQ. ID. NO. 32 CTGCCCCAGGAGTACATCCGCTGGG

SEQ. ID. NO. 40 ATGACACACCTATCTGTGAGGGCTTTC
SEQ. ID. NO. 46 TGCTGGGTGGTGTCTTCTCTGCTA
SEQ. ID. NO. 36 TGCTGGGTGGTGTCTTCTCTGCTA
SEQ. ID. NO. 32 GCGATGCCCTGGGCTGTGGGACCTGT

SEQ. ID. NO. 40 AGGACGCGAACTTAGTTACGTGCTC
SEQ. ID. NO. 46 CTGCATGACCTTTCATCTTTCATTGCC
SEQ. ID. NO. 36 CTGCATGACCTTTCATCTTTCATTGCC
SEQ. ID. NO. 32 CACCATCGCCTGCTCTGGGTGCCCTG

SEQ. ID. NO. 40 CTAACGGGGATTTTTCTCTGTATT
SEQ. ID. NO. 46 AAGCCATCCACGGGCAGTGTGTACCT
SEQ. ID. NO. 36 AAGCCATCCACGGGCAGTGTGTACCT
SEQ. ID. NO. 32 GCCACCCTGTTTGTGCTGGGTGTCT

SEQ. ID. NO. 40 CAATCACGTTTTTTAATGATTGCAAGC
SEQ. ID. NO. 46 TACGGCGTCTTTGGTTTGGGGCACTGC
SEQ. ID. NO. 36 TACGGCGTCTTTGGTTTGGGGCACTGC
SEQ. ID. NO. 32 TTGTGCGGCGACAAATGCCACACCAGT

SEQ. ID. NO. 40 ACCAGATACAATCATATGCTCCTTTC
SEQ. ID. NO. 46 CTTCTCTGTCTGTCTACTCAGCCCTG
SEQ. ID. NO. 36 CTTCTCTGTCTGTCTACTCAGCCCTG
SEQ. ID. NO. 32 GGTC AAGGCCCTCAGGTCGGGAGCTC

SEQ. ID. NO. 40 CGACGGGTCTTCTCTAGGACTTGGCA
SEQ. ID. NO. 46 CTCACCAAGACCAACC GCATTGCAC
SEQ. ID. NO. 36 CTCACCAAGACCAACC GCATTGCAC
SEQ. ID. NO. 32 TGCTACATCCTGTGCTGGGTGGTGTCT

SEQ. ID. NO. 40 TGTGTTTTCAGCTATGCAAGCCCTTCT
SEQ. ID. NO. 46 GCATCTTTCGGTGGGGGCCCGGGAGGG
SEQ. ID. NO. 36 GCATCTTTCGGTGGGGGCCCGGGAGGG
SEQ. ID. NO. 32 TCCTCTGTCTACTGCATGACCTTCA

FIG. 11j.

SUBSTITUTE SHEET (RULE 26)

73/III

SEQ. ID. NO. 40 G A C C A A A A C A A A C C G T A T C C A C C G A
SEQ. ID. NO. 46 T G C C C A G C G G C C A C G C T T C A T C A G T
SEQ. ID. NO. 36 T G C C C A G C G G C C A C G C T T C A T C A G T
SEQ. ID. NO. 32 C T T C A T T G C C A A G C C A T C C A C G G C A

SEQ. ID. NO. 40 A T A T T T G A G C A G G G G A A G A A A T C T G
SEQ. ID. NO. 46 C C T G C C T C A C A G G T G G C C A T C T G C C
SEQ. ID. NO. 36 C C T G C C T C A C A G G T G G C C A T C T G C C
SEQ. ID. NO. 32 G T G T G T A C C T T A C G G C G T C T T G G T T

SEQ. ID. NO. 40 T C A C A G C G C C C A A G T T C A T T A G T C C
SEQ. ID. NO. 46 T G G C A C T T A T C T C G G G C C A G C T G C T
SEQ. ID. NO. 36 T G G C A C T T A T C T C G G G C C A G C T G C T
SEQ. ID. NO. 32 T G G G C A C T G C C T T C T C T G T C T G C T A

SEQ. ID. NO. 40 A G C A T C T C A G C T G G T G A T C A C C T T C
SEQ. ID. NO. 46 C A T C G T G G T C G C C T G G C T G G T G G T G
SEQ. ID. NO. 36 C A T C G T G G T C G C C T G G C T G G T G G T G
SEQ. ID. NO. 32 C T C A G C C C T G C T C A C C A A G A C C A A C

SEQ. ID. NO. 40 A G C C T C A T C T C C G T C C A G C T C C T T G
SEQ. ID. NO. 46 G A G G C A C C G G G C A C A G G C A A G G A G A
SEQ. ID. NO. 36 G A G G C A C C G G G C A C A G G C A A G G A G A
SEQ. ID. NO. 32 C G C A T T G C A C G C A T C T T C G G T G G G G

SEQ. ID. NO. 40 G A G T G T T T G T C T G G T T T G T T G T G G A
SEQ. ID. NO. 46 C A G C C C C C G A A C G G C G G G A G G T G G T
SEQ. ID. NO. 36 C A G C C C C C G A A C G G C G G G A G G T G G T
SEQ. ID. NO. 32 C C C G G G A G G G T G C C C A G C G G C C A C G

SEQ. ID. NO. 40 T C C C C C C A C A T C A T C A T T G A C T A T
SEQ. ID. NO. 46 G A C A C T G C G C T G C A A C C A C C G C G A T
SEQ. ID. NO. 36 G A C A C T G C G C T G C A A C C A C C G C G A T
SEQ. ID. NO. 32 C T T C A T C A G T C C T G C C T C A C A G G T G

SEQ. ID. NO. 40 G G A G A G C A G C G G A C A C T A G A T C C A G
SEQ. ID. NO. 46 G C A A G T A T G T T G G G C T C G C T G G C C T
SEQ. ID. NO. 36 G C A A G T A T G T T G G G C T C G C T G G C C T
SEQ. ID. NO. 32 G C C A T C T G C C T G G C A C T T A T C T C G G

FIG. 11k.

74/III

SEQ. ID. NO. 40 A G A A G G C C A G G G G A G T G C T C A A G T G
SEQ. ID. NO. 46 A C A A T G T G C T C C T C A T C G C G C T C T G
SEQ. ID. NO. 36 A C A A T G T G C T C C T C A T C G C G C T C T G
SEQ. ID. NO. 32 G C C A G C T G C T C A T C G T G G T C G C C T G

SEQ. ID. NO. 40 T G A C A T T T C T G A T C T C T C A C T C A T T
SEQ. ID. NO. 46 C A C G C T T T A T G C C T T C A A G A C T C G C
SEQ. ID. NO. 36 C A C G C T T T A T G C C T T C A A G A C T C G C
SEQ. ID. NO. 32 G C T G G T G G T G G A G G C A C C G G G C A C A

SEQ. ID. NO. 40 T G T T C A C T T T G G A T A C A G T A T C C T C T
SEQ. ID. NO. 46 A A G T G C C C C G A A A A C T T C A A C G A G G
SEQ. ID. NO. 36 A A G T G C C C C G A A A A C T T C A A C G A G G
SEQ. ID. NO. 32 G G C A A G G A G A C A G C C C C G A A C G G C

SEQ. ID. NO. 40 T G A T G G T C A C T T T G T A C T G T T T A T G C
SEQ. ID. NO. 46 C C A A G T T C A T T G G C T T C A C C A T G T A
SEQ. ID. NO. 36 C C A A G T T C A T T G G C T T C A C C A T G T A
SEQ. ID. NO. 32 G G G A G G T G G T G A C A C T G C G C T G C A A

SEQ. ID. NO. 40 C A T T A A A A C G A G A G G T G T C C C A G A G
SEQ. ID. NO. 46 C A C C A C C T G C A T C A T C T G G C T G G C A
SEQ. ID. NO. 36 C A C C A C C T G C A T C A T C T G G C T G G C A
SEQ. ID. NO. 32 C C A C C G C G A T G C A A G T A T G T T G G G C

SEQ. ID. NO. 40 A C T T T C A A T G A A G C C A A A C C T A T T G
SEQ. ID. NO. 46 T T C C T G C C C C A T C T T C T A T G T C A C C T
SEQ. ID. NO. 36 T T C C T G C C C C A T C T T C T A T G T C A C C T
SEQ. ID. NO. 32 T C G C T G G C C T A C A A T G T G C T C C T C A

SEQ. ID. NO. 40 G A T T T A C C A T G T A T A C C A C C T G C A T
SEQ. ID. NO. 46 C C A G T G A C T A C C G G G T A C A G A C C A C
SEQ. ID. NO. 36 C C A G T G A C T A C C G G G T A C A G A C C A C
SEQ. ID. NO. 32 T C G C G C T C T G C A C G C T T T A T G C C T T

SEQ. ID. NO. 40 C A T T T G G T T A G C T T T C A T C C C C A T C
SEQ. ID. NO. 46 C A C C A T G T G C G T G T C A G T C A G C C T C
SEQ. ID. NO. 36 C A C C A T G T G C G T G T C A G T C A G C C T C
SEQ. ID. NO. 32 C A A T A C T C G C A A G T G C C C C G A A A A C

FIG. 1/L.

SUBSTITUTE SHEET (RULE 26)

75/III

SEQ. ID. NO. 40 T T T T T T G G T A C A G C C C A G T C A G C A G
SEQ. ID. NO. 46 A G C G G C T C C G T G G T G C T T G G C T G C C
SEQ. ID. NO. 36 A G C G G C T C C G T G G T G C T T G G C T G C C
SEQ. ID. NO. 32 T T C A A C G A G G C C A A G T T C A T T G G C T

SEQ. ID. NO. 40 A A A A G A T G T A C A T C C A G A C A A C A A C
SEQ. ID. NO. 46 T C T T T G C G C C C A A G C T G C A C A T C A T
SEQ. ID. NO. 36 T C T T T G C G C C C A A G C T G C A C A T C A T
SEQ. ID. NO. 32 T C A C C A T G T A C A C C A C C T G C A T C A T

SEQ. ID. NO. 40 A C T T A C T G T C T C C A T G A G T T T A A G T
SEQ. ID. NO. 46 C C T C T T C C A G C C G C A G A A G A A C A C C
SEQ. ID. NO. 36 C C T C T T C C A G C C G C A G A A G A A C A C C
SEQ. ID. NO. 32 C T G G C T G G C A T T G T T G C C C A T C T T C

SEQ. ID. NO. 40 G C T T C A G T A T C T C T G G G C A T G C T C T
SEQ. ID. NO. 46 A T C G A G G A G G T G C G T T G C A G C A C C G
SEQ. ID. NO. 36 A T C G A G G A G G T G C G T T G C A G C A C C G
SEQ. ID. NO. 32 T A T G T C A C C T C C A G T G A C T A C C G G G

SEQ. ID. NO. 40 A T A T G C C C A A G G T T T A T A T T A T A A T
SEQ. ID. NO. 46 C A G C T C A C G C T T T C A A G G T G G C T G C
SEQ. ID. NO. 36 C A G C T C A C G C T T T C A A G G T G G C T G C
SEQ. ID. NO. 32 T A C A G A C C A C C A C C A T G T G C G T G T C

SEQ. ID. NO. 40 T T T T C A T C C A G A A C A G A A T A C C A T C
SEQ. ID. NO. 46 C C G G G C C A C G C T G C G C C G C A G C A A C
SEQ. ID. NO. 36 C C G G G C C A C G C T G C G C C G C A G C A A C
SEQ. ID. NO. 32 A G T C A G C C T C A G C G G C T C C G T G G T G

SEQ. ID. NO. 40 G A G G A G G T G C G T T G C A G C A C C G C A G
SEQ. ID. NO. 46 G T C T C C C G C A A G C G G T C C A G C A G C C
SEQ. ID. NO. 36 G T C T C C C G C A A G C G G T C C A G C A G C C
SEQ. ID. NO. 32 C T T G G C T G C C T C T T T G C G C C C A A G C

SEQ. ID. NO. 40 C T C A C G C T T T C A A G G T G G C T G C C C G
SEQ. ID. NO. 46 T T G G A G G C T C C A C G G G A T C C A C C C C
SEQ. ID. NO. 36 T T G G A G G C T C C A C G G G A T C C A C C C C
SEQ. ID. NO. 32 T G C A C A T C A T C C T C T T C C A G C C G C A

FIG. 1 Im.

SUBSTITUTE SHEET (RULE 26)

76/III

SEQ. ID. NO. 40 G G C C A C G C T G C G C C G C A G C A A C G T C
SEQ. ID. NO. 46 C T C C T C C T C C A T C A G C A G C A A G A G C
SEQ. ID. NO. 36 C T C C T C C T C C A T C A G C A G C A A G A G C
SEQ. ID. NO. 32 G A A G A A C G T G G T T A G C C A C C G G G C A

SEQ. ID. NO. 40 T C C C G C A A G C G G T C C A G C A G C C T T G
SEQ. ID. NO. 46 A A C A G C G A A G A C C C A T T C C C A C A G C
SEQ. ID. NO. 36 A A C A G C G A A G A C C C A T T C C C A C A G C
SEQ. ID. NO. 32 C C C A C C A G C C G C T T T G G C A G T G C T G

SEQ. ID. NO. 40 G A G G C T C C A C G G G A T C C A C C C C C T C
SEQ. ID. NO. 46 C C G A G A G G C A G A A A G C A G C A G C A G C C
SEQ. ID. NO. 36 C C G A G A G G C A G A A A G C A G C A G C A G C C
SEQ. ID. NO. 32 C T G C C A G G G C C A G C T C C A G C C T T G G

SEQ. ID. NO. 40 C T C C T C C A T C A G C A G C A A G A G C A A C
SEQ. ID. NO. 46 G C T G G C C C T A A C C C A G C A A G A G C A G
SEQ. ID. NO. 36 G C T G G C C C T A A C C C A G C A A G A G C A G
SEQ. ID. NO. 32 C C A A G G G T C T G G C T C C C A G T T T G T C

SEQ. ID. NO. 40 A G C G A A G A C C C A T T C C C A C A G C C C G
SEQ. ID. NO. 46 C A G C A G C A G C C C C T G A C C C T C C C A C
SEQ. ID. NO. 36 C A G C A G C A G C C C C T G A C C C T C C C A C
SEQ. ID. NO. 32 C C C A C T G T T T G C A A T G G C C G T G A G G

SEQ. ID. NO. 40 A G A G G C A G A A A G C A G C A G C A G C C G C T
SEQ. ID. NO. 46 A G C A G C A A C G A T C T C A G C A G C A G C C
SEQ. ID. NO. 36 A G C A G C A A C G A T C T C A G C A G C A G C C
SEQ. ID. NO. 32 T G G T G G A C T C G A C A A C G T C A T C G C T

SEQ. ID. NO. 40 G G C C C T A A C C C A G C A A G A G C A G C A G
SEQ. ID. NO. 46 C A G A T G C A A G C A G A A G G T C A T C T T T
SEQ. ID. NO. 36 C A G A T G C A A G C A G A A G G T C A T C T T T
SEQ. ID. NO. 32 T A T G A C T C T G G A G T C C A T C A T G G C G

SEQ. ID. NO. 40 C A G C A G C C C C T G A C C C T C C C A C A G C
SEQ. ID. NO. 46 G G C A G C G G C A C G G T C A C C T T C T C A C
SEQ. ID. NO. 36 G G C A G C G G C A C G G T C A C C T T C T C A C
SEQ. ID. NO. 32 T G C T G C C T G A G C G A G G A G G C C A A G G

FIG. 1In.

77/III

SEQ. ID. NO. 40 A G C A A C G A T C T C A G C A G C A G C C C A G
SEQ. ID. NO. 46 T G A G C T T T G A T G A G C C T C A G A A G A A
SEQ. ID. NO. 36 T G A G C T T T G A T G A G C C T C A G A A G A A
SEQ. ID. NO. 32 A A G C C C G G C G G A T C A A C G A C G A G A T

SEQ. ID. NO. 40 A T G C A A G C A G A A G G T C A T C T T T G G C
SEQ. ID. NO. 46 C G C C A T G G C C C A C G G G A A T T C T A C G
SEQ. ID. NO. 36 C G C C A T G G C C C A C G G G A A T T C T A C G
SEQ. ID. NO. 32 C G A G C G G C A G C T C C G C A G G G A C A A G

SEQ. ID. NO. 40 A G C G G C A C G G T C A C C T T C T C A C T G A
SEQ. ID. NO. 46 C A C C A G A A C T C C C T G G A G G C C C A G A
SEQ. ID. NO. 36 C A C C A G A A C T C C C T G G A G G C C C A G A
SEQ. ID. NO. 32 C G G G A C G C C C G C C G G G A G C T C A A G C

SEQ. ID. NO. 40 G C T T T G A T G A G C C T C A G A A G A A C G C
SEQ. ID. NO. 46 A A A G C A G C G A T A C G C T G A C C C G A C A
SEQ. ID. NO. 36 A A A G C A G C G A T A C G C T G A C C C G A C A
SEQ. ID. NO. 32 T G C T G C T G C T C G G G A C A G G A G A G A G

SEQ. ID. NO. 40 C A T G G C C C A C G G G A A T T C T A C G C A C
SEQ. ID. NO. 46 C C A G C C A T T A C T C C C G C T G C A G T G C
SEQ. ID. NO. 36 C C A G C C A T T A C T C C C G C T G C A G T G C
SEQ. ID. NO. 32 T G G C A A G A G T A C G T T T A T C A A G C A G

SEQ. ID. NO. 40 C A G A A C T C C C T G G A G G C C C A G A A A A
SEQ. ID. NO. 46 G G G G A A A C G G A C T T A G A T C T G A C C G
SEQ. ID. NO. 36 G G G G A A A C G G A C T T A G A T C T G A C C G
SEQ. ID. NO. 32 A T G A G A A T C A T C C A T G G G T C A G G A T

SEQ. ID. NO. 40 G C A G C G A T A C G C T G A C C C G A C A C C A
SEQ. ID. NO. 46 T C C A G G A A A C A G G T C T G C A A G G A C C
SEQ. ID. NO. 36 T C C A G G A A A C A G G T C T G C A A G G A C C
SEQ. ID. NO. 32 A C T C T G A T G A A G A T A A A A G G G G C T T

SEQ. ID. NO. 40 G C C A T T A C T C C C G C T G C A G T G C G G G
SEQ. ID. NO. 46 T G T G G G T G G A G A C C A G C G G C C A G A G
SEQ. ID. NO. 36 T G T G G G T G G A G A C C A G C G G C C A G A G
SEQ. ID. NO. 32 C A C C A A G C T G G T G T A T C A G A A C A T C

FIG. 110.

SUBSTITUTE SHEET (RULE 26)

78/III

SEQ. ID. NO. 40 G A A A C G G A C T T A G A T C T G A C C G T C C
SEQ. ID. NO. 46 G T G G A G G A C C C T G A A G A G T T G T C C C
SEQ. ID. NO. 36 G T G G A G G A C C C T G A A G A G T T G T C C C
SEQ. ID. NO. 32 T T C A C G G C C A T G C A G G C C A T G A T C A

SEQ. ID. NO. 40 A G G A A A C A G G T C T G C A A G G A C C T G T
SEQ. ID. NO. 46 C A G C A C T T G T A G T G T C C A G T T C A C A
SEQ. ID. NO. 36 C A G C A C T T G T A G T G T C C A G T T C A C A
SEQ. ID. NO. 32 G A G C C A T G G A C A C A C T C A A G A T C C C

SEQ. ID. NO. 40 G G G T G G A G A C C A G C G G C C A G A G G T G
SEQ. ID. NO. 46 G A G C T T T G T C A T C A G T G G T G G A G G C
SEQ. ID. NO. 36 G A G C T T T G T C A T C A G T G G T G G A C G C
SEQ. ID. NO. 32 A T A C A A G T A T G A G C A C A A T A A G G C T

SEQ. ID. NO. 40 G A G G A C C C T G A A G A G T T G T C C C C A G
SEQ. ID. NO. 46 A G C A C T G T T A C A G A A A A C G T A G T G A
SEQ. ID. NO. 36 A G C A C T G T T A C A G A A A A C G T A G T G A
SEQ. ID. NO. 32 C A T G C A C A A T T A G T T C G A G A A G T T G

SEQ. ID. NO. 40 C A C T T G T A G T G T C C A G T T C A C A G A G
SEQ. ID. NO. 46 A T T C A G C G G C C C G C C A T G A C T C T G G A
SEQ. ID. NO. 36 A T T C A A T G A C T C T G G A G T C C A T C A T
SEQ. ID. NO. 32 A T G T G G A G A A G G T G T C T G C T T T T G A

SEQ. ID. NO. 40 C T T T G T C A T C A G T G G T G G A G G C A G C
SEQ. ID. NO. 46 G T C C A T C A T G G C G T G C T G C C T G A G C
SEQ. ID. NO. 36 G G C G T G C T G C C T G A G C G A G G A G G C C
SEQ. ID. NO. 32 G A A T C C A T A T G T A G A T G C A A T A A A G

SEQ. ID. NO. 40 A C T G T T A C A G A A A A C G T A G T G A A T T
SEQ. ID. NO. 46 G A G G A G G C C A A G G A A G C C C G G C G G A
SEQ. ID. NO. 36 A A G G A A G C C C G G C G G A T C A A C G A C G
SEQ. ID. NO. 32 A G T T T A T G G A A T G A T C C T G G A A T C C

SEQ. ID. NO. 40 C A - - - - -
SEQ. ID. NO. 46 T C A A C G A C G A G A T C G A G C G G C A G C T
SEQ. ID. NO. 36 A G A T C G A G C G G C A G C T C C G C A G G G A
SEQ. ID. NO. 32 A G G A A T G C T A T G A T A G A C G A C G A G A

FIG. 11p.

SUBSTITUTE SHEET (RULE 26)

79/111

SEQ. ID. NO. 40 - - - - -
SEQ. ID. NO. 46 C C G C A G G G A C A A G C G G G A C G C C C G C
SEQ. ID. NO. 36 C A A G C G G G A C G C C C G C C G G G A G C T C
SEQ. ID. NO. 32 A T A T C A A T T A T C T G A C T C T A C C A A A

SEQ. ID. NO. 40 - - - - - A T G A C T C T G G
SEQ. ID. NO. 46 C G G G A G C T C A A G C T G C T G C T G C T C G
SEQ. ID. NO. 36 A A G C T G C T G C T G C T C G G G A C A G G A G
SEQ. ID. NO. 32 T A C T A T C T T A A T G A C T T G G A C C G C G

SEQ. ID. NO. 40 A G T C C A T C A T G G C G T G C T G C C T G A G
SEQ. ID. NO. 46 G G A C A G G A G A G A G T G G C A A G A G T A C
SEQ. ID. NO. 36 A G A G T G G C A A G A G T A C G T T T A T C A A
SEQ. ID. NO. 32 T A G C T G A C C C T G C C T A C C T G C C T A C

SEQ. ID. NO. 40 C G A G G A G G C C A A G G A A G C C C G G C G G
SEQ. ID. NO. 46 G T T T A T C A A G C A G A T G A G A A T C A T C
SEQ. ID. NO. 36 G C A G A T G A G A A T C A T C C A T G G G T C A
SEQ. ID. NO. 32 G C A A C A A G A T G T G C T T A G A G T T C G A

SEQ. ID. NO. 40 A T C A A C G A C G A G A T C G A G C G G C A G C
SEQ. ID. NO. 46 C A T G G G T C A G G A T A C T C T G A T G A A G
SEQ. ID. NO. 36 G G A T A C T C T G A T G A A G A T A A A A G G G
SEQ. ID. NO. 32 G T C C C C A C C A C A G G G A T C A T C G A A T

SEQ. ID. NO. 40 T C C G C A G G G A C A A G C G G G A C G C C C G
SEQ. ID. NO. 46 A T A A A A G G G G C T T C A C C A A G C T G G T
SEQ. ID. NO. 36 G C T T C A C C A A G C T G G T G T A T C A G A A
SEQ. ID. NO. 32 A C C C C T T T G A C T T A C A A A G T G T C A T

SEQ. ID. NO. 40 C C G G G A G C T C A A G C T G C T G C T G C T C
SEQ. ID. NO. 46 G T A T C A G A A C A T C T T C A C G G C C A T G
SEQ. ID. NO. 36 C A T C T T C A C G G C C A T G C A G G C C A T G
SEQ. ID. NO. 32 T T T C A G A A T G G T C G A T G T A G G G G G C

SEQ. ID. NO. 40 G G G A C A G G A G A G A G T G G C A A G A G T A
SEQ. ID. NO. 46 C A G G C C A T G A T C A G A G C C A T G G A C A
SEQ. ID. NO. 36 A T C A G A G C C A T G G A C A C A C T C A A G A
SEQ. ID. NO. 32 C A A A G G T C A G A G A G A A G A A A A T G G A

FIG. 11q.

SUBSTITUTE SHEET (RULE 26)

80/III

SEQ. ID. NO. 40 C G T T T A T C A A G C A G A T G A G A A T C A T
SEQ. ID. NO. 46 C A C T C A A G A T C C C A T A C A A G T A T G A
SEQ. ID. NO. 36 T C C C A T A C A A G T A T G A G C A C A A T A A
SEQ. ID. NO. 32 T A C A C T G C T T T G A A A A T G T C A C C T C

SEQ. ID. NO. 40 C C A T G G G T C A G G A T A C T C T G A T G A A
SEQ. ID. NO. 46 G C A C A A T A A G G C T C A T G C A C A A T T A
SEQ. ID. NO. 36 G G C T C A T G C A C A A T T A G T T C G A G A A
SEQ. ID. NO. 32 T A T C A T G T T T C T A G T A G C G C T T A G T

SEQ. ID. NO. 40 G A T A A A A G G G G C T T C A C C A A G C T G G
SEQ. ID. NO. 46 G T T C G A G A A G T T G A T G T G G A G A A G G
SEQ. ID. NO. 36 G T T G A T G T G G A G A A G G T G T C T G C T T
SEQ. ID. NO. 32 G A A T A T G A T C A A G T T C T C G T G G A G T

SEQ. ID. NO. 40 T G T A T C A G A A C A T C T T C A C G G C C A T
SEQ. ID. NO. 46 T G T C T G C T T T T G A G A A T C C A T A T G T
SEQ. ID. NO. 36 T T G A G A A T C C A T A T G T A G A T G C A A T
SEQ. ID. NO. 32 C A G A C A A T G A G A A C C G A A T G G A G G A

SEQ. ID. NO. 40 G C A G G C C A T G A T C A G A G C C A T G G A C
SEQ. ID. NO. 46 A G A T G C A A T A A A G A G T T T A T G G A A T
SEQ. ID. NO. 36 A A A G A G T T T A T G G A A T G A T C C T G G A
SEQ. ID. NO. 32 A A G C A A G G C T C T C T T T A G A A C A A T T

SEQ. ID. NO. 40 A C A C T C A A G A T C C C A T A C A A G T A T G
SEQ. ID. NO. 46 G A T C C T G G A A T C C A G G A A T G C T A T G
SEQ. ID. NO. 36 A T C C A G G A A T G C T A T G A T A G A C G A C
SEQ. ID. NO. 32 A T C A C A T A C C C C T G G T T C C A G A A C T

SEQ. ID. NO. 40 A G C A C A A T A A G G C T C A T G C A C A A T T
SEQ. ID. NO. 46 A T A G A C G A C G A G A A T A T C A A T T A T C
SEQ. ID. NO. 36 G A G A A T A T C A A T T A T C T G A C T C T A C
SEQ. ID. NO. 32 C C T C G G T T A T T C T G T T C T T A A A C A A

SEQ. ID. NO. 40 A G T T C G A G A A G T T G A T G T G G A G A A G
SEQ. ID. NO. 46 T G A C T C T A C C A A A T A C T A T C T T A A T
SEQ. ID. NO. 36 C A A A T A C T A T C T T A A T G A C T T G G A C
SEQ. ID. NO. 32 G A A A G A T C T T C T A G A G G A G A A A A T C

FIG. 11r.

81/III

SEQ. ID. NO. 40 G T G T C T G C T T T T G A G A A T C C A T A T G
SEQ. ID. NO. 46 G A C T T G G A C C G C G T A G C T G A C C C T G
SEQ. ID. NO. 36 C G C G T A G C T G A C C C T G C C T A C C T G C
SEQ. ID. NO. 32 A T G T A T T C C C A T C T A G T C G A C T A C T

SEQ. ID. NO. 40 T A G A T G C A A T A A A G A G T T T A T G G A A
SEQ. ID. NO. 46 C C T A C C T G C C T A C G C A A C A A G A T G T
SEQ. ID. NO. 36 C T A C G C A A C A A G A T G T G C T T A G A G T
SEQ. ID. NO. 32 T C C C A G A A T A T G A T G G A C C C C A G A G

SEQ. ID. NO. 40 T G A T C C T G G A A T C C A G G A A T G C T A T
SEQ. ID. NO. 46 G C T T A G A G T T C G A G T C C C C A C C A C A
SEQ. ID. NO. 36 T C G A G T C C C C A C C A C A G G G A T C A T C
SEQ. ID. NO. 32 A G A T G C C C A G G C A G C C C G A G A A T T C

SEQ. ID. NO. 40 G A T A G A C G A C G A G A A T A T C A A T T A T
SEQ. ID. NO. 46 G G G A T C A T C G A A T A C C C C T T T G A C T
SEQ. ID. NO. 36 G A A T A C C C C T T T G A C T T A C A A A G T G
SEQ. ID. NO. 32 A T T C T G A A G A T G T T C G T G G A C C T G A

SEQ. ID. NO. 40 C T G A C T C T A C C A A A T A C T A T C T T A A
SEQ. ID. NO. 46 T A C A A A G T G T C A T T T T C A G A A T G G T
SEQ. ID. NO. 36 T C A T T T T C A G A A T G G T C G A T G T A G G
SEQ. ID. NO. 32 A C C C A G A C A G T G A C A A A A T T A T C T A

SEQ. ID. NO. 40 T G A C T T G G A C C G C G T A G C T G A C C C T
SEQ. ID. NO. 46 C G A T G T A G G G G G C C A A A G G T C A G A G
SEQ. ID. NO. 36 G G G C C A A A G G T C A G A G A G A A G A A A A
SEQ. ID. NO. 32 C T C C C A C T T C A C G T G C G C C A C A G A C

SEQ. ID. NO. 40 G C C T A C C T G C C T A C G C A A C A A G A T G
SEQ. ID. NO. 46 A G A A G A A A A T G G A T A C A C T G C T T T G
SEQ. ID. NO. 36 T G G A T A C A C T G C T T T G A A A A T G T C A
SEQ. ID. NO. 32 A C C G A G A A T A T C C G C T T T G T C T T T G

SEQ. ID. NO. 40 T G C T T A G A G T T C G A G T C C C C A C C A C
SEQ. ID. NO. 46 A A A A T G T C A C C T C T A T C A T G T T T C T
SEQ. ID. NO. 36 C C T C T A T C A T G T T T C T A G T A G C G C T
SEQ. ID. NO. 32 C T G C C G T C A A G G A C A C C A T C C T C C A

FIG. 1/Is.

SUBSTITUTE SHEET (RULE 26)

82/III

SEQ. ID. NO. 40 A G G G A T C A T C G A A T A C C C C T T T G A C
SEQ. ID. NO. 46 A G T A G C G C T T A G T G A A T A T G A T C A A
SEQ. ID. NO. 36 T A G T G A A T A T G A T C A A G T T C T C G T G
SEQ. ID. NO. 32 G T T G A A C C T G A A G G A C T G C G G T C T G

SEQ. ID. NO. 40 T T A C A A A G T G T C A T T T T C A G A A T G G
SEQ. ID. NO. 46 G T T C T C G T G G A G T C A G A C A A T G A G A
SEQ. ID. NO. 36 G A G T C A G A C A A T G A G A A C C G A A T G G
SEQ. ID. NO. 32 T T C T A A

SEQ. ID. NO. 40 T C G A T G T A G G G G G C C A A A G G T C A G A
SEQ. ID. NO. 46 A C C G A A T G G A G G A A A G C A A G G C T C T
SEQ. ID. NO. 36 A G G A A A G C A A G G C T C T C T T T A G A A C
SEQ. ID. NO. 32

SEQ. ID. NO. 40 G A G A A G A A A A T G G A T A C A C T G C T T T
SEQ. ID. NO. 46 C T T T A G A A C A A T T A T C A C A T A C C C C
SEQ. ID. NO. 36 A A T T A T C A C A T A C C C C T G G T T C C A G
SEQ. ID. NO. 32

SEQ. ID. NO. 40 G A A A A T G T C A C C T C T A T C A T G T T T C
SEQ. ID. NO. 46 T G G T T C C A G A A C T C C T C G G T T A T T C
SEQ. ID. NO. 36 A A C T C C T C G G T T A T T C T G T T C T T A A
SEQ. ID. NO. 32

SEQ. ID. NO. 40 T A G T A G C G C T T A G T G A A T A T G A T C A
SEQ. ID. NO. 46 T G T T C T T A A A C A A G A A A G A T C T T C T
SEQ. ID. NO. 36 A C A A G A A A G A T C T T C T A G A G G A G A A
SEQ. ID. NO. 32

SEQ. ID. NO. 40 A G T T C T C G T G G A G T C A G A C A A T G A G
SEQ. ID. NO. 46 A G A G G A G A A A A T C A T G T A T T C C C A T
SEQ. ID. NO. 36 A A T C A T G T A T T C C C A T C T A G T C G A C
SEQ. ID. NO. 32

SEQ. ID. NO. 40 A A C C G A A T G G A G G A A A G C A A G G C T C
SEQ. ID. NO. 46 C T A G T C G A C T A C T T C C C A G A A T A T G
SEQ. ID. NO. 36 T A C T T C C C A G A A T A T G A T G G A C C C C
SEQ. ID. NO. 32

FIG. 11t.

SUBSTITUTE SHEET (RULE 26)

83/III

SEQ. ID. NO. 40 T C T T T A G A A C A A T T A T C A C A T A C C C
SEQ. ID. NO. 46 A T G G A C C C C A G A G A G A T G C C C A G G C
SEQ. ID. NO. 36 A G A G A G A T G C C C A G G C A G C C C G A G A
SEQ. ID. NO. 32

SEQ. ID. NO. 40 C T G G T T C C A G A A C T C C T C G G T T A T T
SEQ. ID. NO. 46 A G C C C G A G A A T T C A T T C T G A A G A T G
SEQ. ID. NO. 36 A T T C A T T C T G A A G A T G T T C G T G G A C
SEQ. ID. NO. 32

SEQ. ID. NO. 40 C T G T T C T T A A A C A A G A A A G A T C T T C
SEQ. ID. NO. 46 T T C G T G G A C C T G A A C C C A G A C A G T G
SEQ. ID. NO. 36 C T G A A C C C A G A C A G T G A C A A A A T T A
SEQ. ID. NO. 32

SEQ. ID. NO. 40 T A G A G G A G A A A A T C A T G T A T T C C C A
SEQ. ID. NO. 46 A C A A A A T T A T C T A C T C C C A C T T C A C
SEQ. ID. NO. 36 T C T A C T C C C A C T T C A C G T G C G C C A C
SEQ. ID. NO. 32

SEQ. ID. NO. 40 T C T A G T C G A C T A C T T C C C A G A A T A T
SEQ. ID. NO. 46 G T G C G C C A C A G A C A C C G A G A A T A T C
SEQ. ID. NO. 36 A G A C A C C G A G A A T A T C C G C T T T G T C
SEQ. ID. NO. 32

SEQ. ID. NO. 40 G A T G G A C C C C A G A G A G A T G C C C A G G
SEQ. ID. NO. 46 C G C T T T G T C T T T G C T G C C G T C A A G G
SEQ. ID. NO. 36 T T T G C T G C C G T C A A G G A C A C C A T C C
SEQ. ID. NO. 32

SEQ. ID. NO. 40 C A G C C C G A G A A T T C A T T C T G A A G A T
SEQ. ID. NO. 46 A C A C C A T C C T C C A G T T G A A C C T G A A
SEQ. ID. NO. 36 T C C A G T T G A A C C T G A A G G A C T G C G G
SEQ. ID. NO. 32

SEQ. ID. NO. 40 G T T C G T G G A C C T G A A C C C A G A C A G T
SEQ. ID. NO. 46 G G A C T G C G G T C T G T T C T A A T T G T G C
SEQ. ID. NO. 36 T C T G T T C T A A
SEQ. ID. NO. 32

FIG. 11u.

SUBSTITUTE SHEET (RULE 26)

84/III

SEQ. ID. NO. 40 G A C A A A A T T A T C T A C T C C C A C T T C A
SEQ. ID. NO. 46 C T C C T A G A C A C C C G C C C T G C C C T T C
SEQ. ID. NO. 36
SEQ. ID. NO. 32

SEQ. ID. NO. 40 C G T G C G C C A C A G A C A C C G A G A A T A T
SEQ. ID. NO. 46 C C T G G T
SEQ. ID. NO. 36
SEQ. ID. NO. 32

SEQ. ID. NO. 40 C C G C T T T G T C T T T G C T G C C G T C A A G
SEQ. ID. NO. 46
SEQ. ID. NO. 36
SEQ. ID. NO. 32

SEQ. ID. NO. 40 G A C A C C A T C C T C C A G T T G A A C C T G A
SEQ. ID. NO. 46
SEQ. ID. NO. 36
SEQ. ID. NO. 32

SEQ. ID. NO. 40 A G G A C T G C G G T C T G T T C T A A
SEQ. ID. NO. 46
SEQ. ID. NO. 36
SEQ. ID. NO. 32

FIG. 1/iv.

85/III

ClustalW Formatted Alignments

SEQ. ID. NO. 41 M V C E G K R S A S C P C F F L L T A K F Y W I L
 SEQ. ID. NO. 47 M G S L L A L P A L L L L W G A V A E G P A K K V
 SEQ. ID. NO. 37 M G S L L A L P A L L L L W G A V A E G P A K K V
 SEQ. ID. NO. 33 M A F Y S C C W V L L A L T W H T S A Y G P D Q R

SEQ. ID. NO. 41 T M M Q R T H S Q E Y A H S I R V D G D I I L G G
 SEQ. ID. NO. 47 L T L E G D L V L G G L F P V H Q K G G P A E D C
 SEQ. ID. NO. 37 L T L E G D L V L G G L F P V H Q K G G P A E D C
 SEQ. ID. NO. 33 A Q K K G D I I L G G L F P I H F G V A A K D Q D

SEQ. ID. NO. 41 L F P V H A K G E R G V P C G E L K K E K G I H R
 SEQ. ID. NO. 47 G P V N E H R G I Q R L E A M L F A L D R I N R D
 SEQ. ID. NO. 37 G P V N E H R G I Q R L E A M L F A L D R I N R D
 SEQ. ID. NO. 33 L K S R P E S V E C I R Y N F R G F R W L Q A M I

SEQ. ID. NO. 41 L E A M L Y A I D Q I N K D P D L L S N I T L G V
 SEQ. ID. NO. 47 P H L L P G V R L G A H I L D S C S K D T H A L E
 SEQ. ID. NO. 37 P H L L P G V R L G A H I L D S C S K D T H A L E
 SEQ. ID. NO. 33 F A I E E I N S S P A L L P N L T L G Y R I F D T

SEQ. ID. NO. 41 R I L D T C S R D T Y A L E Q S L T F V Q A L I E
 SEQ. ID. NO. 47 Q A L D F V R A S L S R G A D G S R H I C P D G S
 SEQ. ID. NO. 37 Q A L D F V R A S L S R G A D G S R H I C P D G S
 SEQ. ID. NO. 33 C N T V S K A L E A T L S F V A Q N K I D S L N L

SEQ. ID. NO. 41 K D A S D V K C A N G D P P I F T K P D K I S G V
 SEQ. ID. NO. 47 Y A T H G D A P T A I T G V I G G S Y S D V S I Q
 SEQ. ID. NO. 37 Y A T H G D A P T A I T G V I G G S Y S D V S I Q
 SEQ. ID. NO. 33 D E F C N C S E H I P S T I A V V G A T G S G V S

SEQ. ID. NO. 41 I G A A A S S V S I M V A N I L R L F K I P Q I S
 SEQ. ID. NO. 47 V A N L L R L F Q I P Q I S Y A S T S A K L S D K
 SEQ. ID. NO. 37 V A N L L R L F Q I P Q I S Y A S T S A K L S D K
 SEQ. ID. NO. 33 T A V A N L L G L F Y I P Q V S Y A S S S R L L S

SEQ. ID. NO. 41 Y A S T A P E L S D N T R Y D F F S R V V P P D S
 SEQ. ID. NO. 47 S R Y D Y F A R T V P P D F F Q A K A M A E I L R
 SEQ. ID. NO. 37 S R Y D Y F A R T V P P D F F Q A K A M A E I L R
 SEQ. ID. NO. 33 N K N Q F K S F L R T I P N D E H Q A T A M A D I

FIG. 12a.

SUBSTITUTE SHEET (RULE 26)

86/III

SEQ. ID. NO. 41 YQAQAMVDIVTALGWNYVSTLASEG
 SEQ. ID. NO. 47 FFNWTYVSTVASEGDYGETGIEAFE
 SEQ. ID. NO. 37 FFNWTYVSTVASEGDYGETGIEAFE
 SEQ. ID. NO. 33 IEYFRWNWVGTTAAADDDYGRPGIEK

SEQ. ID. NO. 41 NYGESGVEAFTQISREIGGVCIAQS
 SEQ. ID. NO. 47 LEARARNICVATSEKVGGRAMSRAAF
 SEQ. ID. NO. 37 LEARARNICVATSEKVGGRAMSRAAF
 SEQ. ID. NO. 33 FREEAEERDIDIDFSELISQYSDEE

SEQ. ID. NO. 41 QKIPREPRPGEFEKI IKRLLET PNA
 SEQ. ID. NO. 47 EGVVRALLQKPSARVAVLFT RSEDA
 SEQ. ID. NO. 37 EGVVRALLQKPSARVAVLFT RSEDA
 SEQ. ID. NO. 33 EIQHVVEVIQNSTAKVIVVVFSSGPD

SEQ. ID. NO. 41 RAVIMFANEDDIRRILEAAKKLNQS
 SEQ. ID. NO. 47 REL LAASQRLNASFTWVASD GWGAL
 SEQ. ID. NO. 37 REL LAASQRLNASFTWVASD GWGAL
 SEQ. ID. NO. 33 LEPLIKEIVRRNITGKIWLASEAWA

SEQ. ID. NO. 41 GHFLWIGSDSWGSKIAPVYQQEEIA
 SEQ. ID. NO. 47 ESVVAGSEGA AEGAITIELASYPIS
 SEQ. ID. NO. 37 ESVVAGSEGA AEGAITIELASYPIS
 SEQ. ID. NO. 33 SSSLIAM PQYFHVVG GTIGFALKAG

SEQ. ID. NO. 41 EGAVTILPKRASIDGFDRYFRSRTL
 SEQ. ID. NO. 47 DFASYFQSLDPWNNSRNPWFREFWE
 SEQ. ID. NO. 37 DFASYFQSLDPWNNSRNPWFREFWE
 SEQ. ID. NO. 33 QIPGFRREFLKKVHPRKSVHNGFAKE

SEQ. ID. NO. 41 ANNRRNVWF AEFWEENFGCKLGSHG
 SEQ. ID. NO. 47 QRFRC SFRQRDCAAHSLRAVPFEQE
 SEQ. ID. NO. 37 QRFRC SFRQRDCAAHSLRAVPFEQE
 SEQ. ID. NO. 33 FWEETFNCHLQEGAKGPLPVDTFLR

SEQ. ID. NO. 41 KRNSHIKKCTGLER IARDSSSYEQEG
 SEQ. ID. NO. 47 SKIMFVVNAVYAMAHALHNMHRA LC
 SEQ. ID. NO. 37 SKIMFVVNAVYAMAHALHNMHRA LC
 SEQ. ID. NO. 33 GHEESGDRFSNSSTAFRPLCTG DEN

FIG. 12b.

SUBSTITUTE SHEET (RULE 26)

87/III

SEQ. ID. NO. 41 K V Q F V I D A V Y S M A Y A L H N M H K D L C P
 SEQ. ID. NO. 47 P N T T R L C D A M R P V N G R R L Y K D F V L N
 SEQ. ID. NO. 37 P N T T R L C D A M R P V N G R R L Y K D F V L N
 SEQ. ID. NO. 33 I S S V E T P Y I D Y T H L R I S Y N V Y L A V Y

SEQ. ID. NO. 41 G Y I G L C P R M S T I D G K E L L G Y I R A V N
 SEQ. ID. NO. 47 V K F D A P F R P A D T H N E V R F D R F G D G I
 SEQ. ID. NO. 37 V K F D A P F R P A D T H N E V R F D R F G D G I
 SEQ. ID. NO. 33 S I A H A L Q D I Y T C L P G R G L F T N G S C A

SEQ. ID. NO. 41 F N G S A G T P V T F N E N G D A P G R Y D I F Q
 SEQ. ID. NO. 47 G R Y N I F T Y L R A G S G R Y R Y Q K V G Y W A
 SEQ. ID. NO. 37 G R Y N I F T Y L R A G S G R Y R Y Q K V G Y W A
 SEQ. ID. NO. 33 D I K K V E A W Q V L K H L R H L N F T N N M G E

SEQ. ID. NO. 41 Y Q I T N K S T E Y K V I G H W T N Q L H L K V E
 SEQ. ID. NO. 47 E G L T L D T S L I P W A S P S A G P L P A S R C
 SEQ. ID. NO. 37 E G L T L D T S L I P W A S P S A G P L P A S R C
 SEQ. ID. NO. 33 Q V T F D E C G D L V G N Y S I I N W H L S P E D

SEQ. ID. NO. 41 D M Q W A H R E H T H P A S V C S L P C K P G E R
 SEQ. ID. NO. 47 S E P C L Q N E V K S V Q P G E V C C W L C I P C
 SEQ. ID. NO. 37 S E P C L Q N E V K S V Q P G E V C C W L C I P C
 SEQ. ID. NO. 33 G S I V F K E V G Y Y N V Y A K K G E R L F I N E

SEQ. ID. NO. 41 K K T V K G V P C C W H C E R C E G Y N Y Q V D E
 SEQ. ID. NO. 47 Q P Y E Y R L D E F T C A D C G L G Y W P N A S L
 SEQ. ID. NO. 37 Q P Y E Y R L D E F T C A D C G L G Y W P N A S L
 SEQ. ID. NO. 33 E K I L W S G F S R E V P F S N C S R D C L A G T

SEQ. ID. NO. 41 L S C E L C P L D Q R P N M N R T G C Q L I P I I
 SEQ. ID. NO. 47 T G C F E L P Q E Y I R W G D A W A V G P V T I A
 SEQ. ID. NO. 37 T G C F E L P Q E Y I R W G D A W A V G P V T I A
 SEQ. ID. NO. 33 R K G I I E G E P T C C F E C V E C P D G E Y S D

SEQ. ID. NO. 41 K L E W H S P W A V V P V F V A I L G I I A T T F
 SEQ. ID. NO. 47 C L G A L A T L F V L G V F V R H N A T P V V K A
 SEQ. ID. NO. 37 C L G A L A T L F V L G V F V R H N A T P V V K A
 SEQ. ID. NO. 33 E T D A S A C N K C P D D F W S N E N H T S C F E

FIG. 12c.

SUBSTITUTE SHEET (RULE 26)

88/III

SEQ. ID. NO. 41 V I V T F V R Y N D T P I V R A S G R E L S Y V L
 SEQ. ID. NO. 47 S G R E L C Y I L L G G V F L C Y C M T F I F I A
 SEQ. ID. NO. 37 S G R E L C Y I L L G G V F L C Y C M T F I F I A
 SEQ. ID. NO. 33 L P Q E Y I R W G D A W A V G P V T I A C L G A L

SEQ. ID. NO. 41 L T G I F L C Y S I T F L M I A A P D T I I C S F
 SEQ. ID. NO. 47 K P S T A V C T L R R L G L G T A F S V C Y S A L
 SEQ. ID. NO. 37 K P S T A V C T L R R L G L G T A F S V C Y S A L
 SEQ. ID. NO. 33 A T L F V L G V F V R H N A T P V V K A S G R E L

SEQ. ID. NO. 41 R R V F L G L G M C F S Y A A L L T K T N R I H R
 SEQ. ID. NO. 47 L T K T N R I A R I F G G A R E G A Q R P R F I S
 SEQ. ID. NO. 37 L T K T N R I A R I F G G A R E G A Q R P R F I S
 SEQ. ID. NO. 33 C Y I L L G G V F L C Y C M T F I F I A K P S T A

SEQ. ID. NO. 41 I F E Q G K K S V T A P K F I S P A S Q L V I T F
 SEQ. ID. NO. 47 P A S Q V A I C L A L I S G Q L L I V V A W L V V
 SEQ. ID. NO. 37 P A S Q V A I C L A L I S G Q L L I V V A W L V V
 SEQ. ID. NO. 33 V C T L R R L G L G T A F S V C Y S A L L T K T N

SEQ. ID. NO. 41 S L I S V Q L L G V F V W F V V D P P H I I I D Y
 SEQ. ID. NO. 47 E A P G T G K E T A P E R R E V V T L R C N H R D
 SEQ. ID. NO. 37 E A P G T G K E T A P E R R E V V T L R C N H R D
 SEQ. ID. NO. 33 R I A R I F G G A R E G A Q R P R F I S P A S Q V

SEQ. ID. NO. 41 G E Q R T L D P E K A R G V L K C D I S D L S L I
 SEQ. ID. NO. 47 A S M L G S L A Y N V L L I A L C T L Y A F K T R
 SEQ. ID. NO. 37 A S M L G S L A Y N V L L I A L C T L Y A F K T R
 SEQ. ID. NO. 33 A I C L A L I S G Q L L I V V A W L V V E A P G T

SEQ. ID. NO. 41 C S L G Y S I L L M V T C T V Y A I K T R G V P E
 SEQ. ID. NO. 47 K C P E N F N E A K F I G F T M Y T T C I I W L A
 SEQ. ID. NO. 37 K C P E N F N E A K F I G F T M Y T T C I I W L A
 SEQ. ID. NO. 33 G K E T A P E R R E V V T L R C N H R D A S M L G

SEQ. ID. NO. 41 T F N E A K P I G F T M Y T T C I I W L A F I P I
 SEQ. ID. NO. 47 F L P I F Y V T S S D Y R V Q T T T M C V S V S L
 SEQ. ID. NO. 37 F L P I F Y V T S S D Y R V Q T T T M C V S V S L
 SEQ. ID. NO. 33 S L A Y N V L L I A L C T L Y A F N T R K C P E N

FIG. 12d.

SUBSTITUTE SHEET (RULE 26)

89/111

SEQ. ID. NO. 41 F F G T A Q S A E K M Y I Q T T T L T V S M S L S
 SEQ. ID. NO. 47 S G S V V L G C L F A P K L H I I L F Q P Q K N T
 SEQ. ID. NO. 37 S G S V V L G C L F A P K L H I I L F Q P Q K N T
 SEQ. ID. NO. 33 F N E A K F I G F T M Y T T C I I W L A L L P I F

SEQ. ID. NO. 41 A S V S L G M L Y M P K V Y I I I F H P E Q N T I
 SEQ. ID. NO. 47 I E E V R C S T A A H A F K V A A R A T L R R S N
 SEQ. ID. NO. 37 I E E V R C S T A A H A F K V A A R A T L R R S N
 SEQ. ID. NO. 33 Y V T S S D Y R V Q T T T M C V S V S L S G S V V

SEQ. ID. NO. 41 E E V R C S T A A H A F K V A A R A T L R R S N V
 SEQ. ID. NO. 47 V S R K R S S S L G G S T G S T P S S S I S S K S
 SEQ. ID. NO. 37 V S R K R S S S L G G S T G S T P S S S I S S K S
 SEQ. ID. NO. 33 L G C L F A P K L H I I L F Q P Q K N V V S H R A

SEQ. ID. NO. 41 S R K R S S S L G G S T G S T P S S S I S S K S N
 SEQ. ID. NO. 47 N S E D P F P Q P E R Q K Q Q Q P L A L T Q Q E Q
 SEQ. ID. NO. 37 N S E D P F P Q P E R Q K Q Q Q P L A L T Q Q E Q
 SEQ. ID. NO. 33 P T S R F G S A A A R A S S S L G Q G S G S Q F V

SEQ. ID. NO. 41 S E D P F P Q P E R Q K Q Q Q P L A L T Q Q E Q Q
 SEQ. ID. NO. 47 Q Q Q P L T L P Q Q Q R S Q Q Q P R C K Q K V I F
 SEQ. ID. NO. 37 Q Q Q P L T L P Q Q Q R S Q Q Q P R C K Q K V I F
 SEQ. ID. NO. 33 P T V C N G R E V V D S T T S S L M T L E S I M A

SEQ. ID. NO. 41 Q Q P L T L P Q Q Q R S Q Q Q P R C K Q K V I F G
 SEQ. ID. NO. 47 G S G T V T F S L S F D E P Q K N A M A H G N S T
 SEQ. ID. NO. 37 G S G T V T F S L S F D E P Q K N A M A H G N S T
 SEQ. ID. NO. 33 C C L S E E A K E A R R I N D E I E R Q L R R D K

SEQ. ID. NO. 41 S G T V T F S L S F D E P Q K N A M A H G N S T H
 SEQ. ID. NO. 47 H Q N S L E A Q K S S D T L T R H Q P L L P L Q C
 SEQ. ID. NO. 37 H Q N S L E A Q K S S D T L T R H Q P L L P L Q C
 SEQ. ID. NO. 33 R D A R R E L K L L L L G T G E S G K S T F I K Q

SEQ. ID. NO. 41 Q N S L E A Q K S S D T L T R H Q P L L P L Q C G
 SEQ. ID. NO. 47 G E T D L D L T V Q E T G L Q G P V G G D Q R P E
 SEQ. ID. NO. 37 G E T D L D L T V Q E T G L Q G P V G G D Q R P E
 SEQ. ID. NO. 33 M R I I H G S G Y S D E D K R G F T K L V Y Q N I

FIG. 12e.

SUBSTITUTE SHEET (RULE 26)

90/III

SEQ. ID. NO. 41 E T D L D L T V Q E T G L Q G P V G G D Q R P E V
 SEQ. ID. NO. 47 V E D P E E L S P A L V V S S S Q S F V I S G G G
 SEQ. ID. NO. 37 V E D P E E L S P A L V V S S S Q S F V I S G G G
 SEQ. ID. NO. 33 F T A M Q A M I R A M D T L K I P Y K Y E H N K A

SEQ. ID. NO. 41 E D P E E L S P A L V V S S S Q S F V I S G G G S
 SEQ. ID. NO. 47 S T V T E N V V N S A A A M T L E S I M A C C L S
 SEQ. ID. NO. 37 S T V T E N V V N S M T L E S I M A C C L S E E A
 SEQ. ID. NO. 33 H A Q L V R E V D V E K V S A F E N P Y V D A I K

SEQ. ID. NO. 41 T V T E N V V N S M T L E S I M A C C L S E E A K
 SEQ. ID. NO. 47 E E A K E A R R I N D E I E R Q L R R D K R D A R
 SEQ. ID. NO. 37 K E A R R I N D E I E R Q L R R D K R D A R R E L
 SEQ. ID. NO. 33 S L W N D P G I Q E C Y D R R R E Y Q L S D S T K

SEQ. ID. NO. 41 E A R R I N D E I E R Q L R R D K R D A R R E L K
 SEQ. ID. NO. 47 R E L K L L L L G T G E S G K S T F I K Q M R I I
 SEQ. ID. NO. 37 K L L L L G T G E S G K S T F I K Q M R I I H G S
 SEQ. ID. NO. 33 Y Y L N D L D R V A D P A Y L P T Q Q D V L R V R

SEQ. ID. NO. 41 L L L L G T G E S G K S T F I K Q M R I I H G S G
 SEQ. ID. NO. 47 H G S G Y S D E D K R G F T K L V Y Q N I F T A M
 SEQ. ID. NO. 37 G Y S D E D K R G F T K L V Y Q N I F T A M Q A M
 SEQ. ID. NO. 33 V P T T G I I E Y P F D L Q S V I F R M V D V G G

SEQ. ID. NO. 41 Y S D E D K R G F T K L V Y Q N I F T A M Q A M I
 SEQ. ID. NO. 47 Q A M I R A M D T L K I P Y K Y E H N K A H A Q L
 SEQ. ID. NO. 37 I R A M D T L K I P Y K Y E H N K A H A Q L V R E
 SEQ. ID. NO. 33 Q R S E R R K W I H C F E N V T S I M F L V A L S

SEQ. ID. NO. 41 R A M D T L K I P Y K Y E H N K A H A Q L V R E V
 SEQ. ID. NO. 47 V R E V D V E K V S A F E N P Y V D A I K S L W N
 SEQ. ID. NO. 37 V D V E K V S A F E N P Y V D A I K S L W N D P G
 SEQ. ID. NO. 33 E Y D Q V L V E S D N E N R M E E S K A L F R T I

SEQ. ID. NO. 41 D V E K V S A F E N P Y V D A I K S L W N D P G I
 SEQ. ID. NO. 47 D P G I Q E C Y D R R R E Y Q L S D S T K Y Y L N
 SEQ. ID. NO. 37 I Q E C Y D R R R E Y Q L S D S T K Y Y L N D L D
 SEQ. ID. NO. 33 I T Y P W F Q N S S V I L F L N K K D L L E E K I

FIG. 12f.

SUBSTITUTE SHEET (RULE 26)

91/III

SEQ. ID. NO. 41 Q E C Y D R R R E Y Q L S D S T K Y Y L N D L D R
 SEQ. ID. NO. 47 D L D R V A D P A Y L P T Q Q D V L R V R V P T T
 SEQ. ID. NO. 37 R V A D P A Y L P T Q Q D V L R V R V P T T G I I
 SEQ. ID. NO. 33 M Y S H L V D Y F P E Y D G P Q R D A Q A A R E F

SEQ. ID. NO. 41 V A D P A Y L P T Q Q D V L R V R V P T T G I I E
 SEQ. ID. NO. 47 G I I E Y P F D L Q S V I F R M V D V G G Q R S E
 SEQ. ID. NO. 37 E Y P F D L Q S V I F R M V D V G G Q R S E R R K
 SEQ. ID. NO. 33 I L K M F V D L N P D S D K I I Y S H F T C A T D

SEQ. ID. NO. 41 Y P F D L Q S V I F R M V D V G G Q R S E R R K W
 SEQ. ID. NO. 47 R R K W I H C F E N V T S I M F L V A L S E Y D Q
 SEQ. ID. NO. 37 W I H C F E N V T S I M F L V A L S E Y D Q V L V
 SEQ. ID. NO. 33 T E N I R F V F A A V K D T I L Q L N L K D C G L

SEQ. ID. NO. 41 I H C F E N V T S I M F L V A L S E Y D Q V L V E
 SEQ. ID. NO. 47 V L V E S D N E N R M E E S K A L F R T I I T Y P
 SEQ. ID. NO. 37 E S D N E N R M E E S K A L F R T I I T Y P W F Q
 SEQ. ID. NO. 33 F

SEQ. ID. NO. 41 S D N E N R M E E S K A L F R T I I T Y P W F Q N
 SEQ. ID. NO. 47 W F Q N S S V I L F L N K K D L L E E K I M Y S H
 SEQ. ID. NO. 37 N S S V I L F L N K K D L L E E K I M Y S H L V D
 SEQ. ID. NO. 33

SEQ. ID. NO. 41 S S V I L F L N K K D L L E E K I M Y S H L V D Y
 SEQ. ID. NO. 47 L V D Y F P E Y D G P Q R D A Q A A R E F I L K M
 SEQ. ID. NO. 37 Y F P E Y D G P Q R D A Q A A R E F I L K M F V D
 SEQ. ID. NO. 33

SEQ. ID. NO. 41 F P E Y D G P Q R D A Q A A R E F I L K M F V D L
 SEQ. ID. NO. 47 F V D L N P D S D K I I Y S H F T C A T D T E N I
 SEQ. ID. NO. 37 L N P D S D K I I Y S H F T C A T D T E N I R F V
 SEQ. ID. NO. 33

SEQ. ID. NO. 41 N P D S D K I I Y S H F T C A T D T E N I R F V F
 SEQ. ID. NO. 47 R F V F A A V K D T I L Q L N L K D C G L F
 SEQ. ID. NO. 37 F A A V K D T I L Q L N L K D C G L F
 SEQ. ID. NO. 33

FIG. 12g.

SUBSTITUTE SHEET (RULE 26)

92/III

SEQ. ID. NO. 41 A A V K D T I L Q L N L K D C G L F
SEQ. ID. NO. 47
SEQ. ID. NO. 37
SEQ. ID. NO. 33

FIG. 12h.

93/III

ClustalW Formatted Alignments

SEQ. ID. NO. 44 A T G T T G C T G C T G C T G C T A C T G G C G C
SEQ. ID. NO. 42 A T G G C T T C C C C G C G G A G C T C C G G G C

SEQ. ID. NO. 44 C A C T C T T C C T C C G C C C C C C G G G C G C
SEQ. ID. NO. 42 A G C C C G G G C C G C C G C C G C C G C C G C C

SEQ. ID. NO. 44 G G G C G G G G C G C A G A C C C C C A A C G C C
SEQ. ID. NO. 42 A C C G C C G C C C G C G C G C C T G C T A C T G

SEQ. ID. NO. 44 A C C T C A G A A G G T T G C C A G A T C A T A C
SEQ. ID. NO. 42 C T A C T G C T G C T G C C G C T G C T G C T G C

SEQ. ID. NO. 44 A C C C G C C C T G G G A A G G G G G C A T C A G
SEQ. ID. NO. 42 C T C T G G C G C C C G G G G C C T G G G G C T G

SEQ. ID. NO. 44 G T A C C G G G G C C T G A C T C G G G A C C A G
SEQ. ID. NO. 42 G G C G C G G G G C G C C C C C C G G C C G C C G

SEQ. ID. NO. 44 G T G A A G G C T A T C A A C T T C C T G C C A G
SEQ. ID. NO. 42 C C C A G C A G C C C G C C G C T C T C C A T C A

SEQ. ID. NO. 44 T G G A C T A T G A G A T T G A G T A T G T G T G
SEQ. ID. NO. 42 T G G G C C T C A T G C C G C T C A C C A A G G A

SEQ. ID. NO. 44 C C G G G G G G A G C G C G A G G T G G T G G G G
SEQ. ID. NO. 42 G G T G G C C A A G G G C A G C A T C G G G C G C

SEQ. ID. NO. 44 C C C A A G G T C C G C A A G T G C C T G G C C A
SEQ. ID. NO. 42 G G T G T G C T C C C C G C C G T G G A A C T G G

SEQ. ID. NO. 44 A C G G C T C C T G G A C A G A T A T G G A C A C
SEQ. ID. NO. 42 C C A T C G A G C A G A T C C G C A A C G A G T C

SEQ. ID. NO. 44 A C C C A G C C G C T G T G T C C G A A T C T G C
SEQ. ID. NO. 42 A C T C C T G C G C C C T T A C T T C C T C G A C

FIG. 13a.

SUBSTITUTE SHEET (RULE 26)

94/III

SEQ. ID. NO. 44 T C C A A G T C T T A T T T G A C C C T G G A A A
SEQ. ID. NO. 42 C T G C G G C T C T A T G A C A C G G A G T G C G

SEQ. ID. NO. 44 A T G G G A A G G T T T T C C T G A C G G G T G G
SEQ. ID. NO. 42 A C A A C G C A A A A G G G T T G A A A G C C T T

SEQ. ID. NO. 44 G G A C C T C C C A G C T C T G G A C G G A G C C
SEQ. ID. NO. 42 C T A C G A T G C A A T A A A A T A C G G G G C C G

SEQ. ID. NO. 44 C G G G T G G A T T T C C G G T G T G A C C C C G
SEQ. ID. NO. 42 A A C C A C T T G A T G G T G T T T G G A G G C G

SEQ. ID. NO. 44 A C T T C C A T C T G G T G G G C A G C T C C C G
SEQ. ID. NO. 42 T C T G T C C A T C C G T C A C A T C C A T C A T

SEQ. ID. NO. 44 G A G C A T C T G T A G T C A G G G C C A G T G G
SEQ. ID. NO. 42 T G C A G A G T C C C T C C A A G G C T G G A A T

SEQ. ID. NO. 44 A G C A C C C C C A A G C C C C A C T G C C A G G
SEQ. ID. NO. 42 C T G G T G C A G C T T T T C T T T T G C T G C A A

SEQ. ID. NO. 44 T G A A T C G A A C G C C C A C A C T C A G A A C G
SEQ. ID. NO. 42 C C A C G C C T G T T C T A G C C G A T A A G A A

SEQ. ID. NO. 44 G C G C G C A G T G T A C A T C G G G G C A C T G
SEQ. ID. NO. 42 A A A A T A C C C T T A T T T C T T T C G G A C C

SEQ. ID. NO. 44 T T T C C C A T G A G C G G G G G C T G G C C A G
SEQ. ID. NO. 42 G T C C C A T C A G A C A A T G C G G T G A A T C

SEQ. ID. NO. 44 G G G G C C A G G C C T G C C A G C C C G C G G T
SEQ. ID. NO. 42 C A G C C A T T C T G A A G T T G C T C A A G C A

SEQ. ID. NO. 44 G G A G A T G G C G C T G G A G G A C G T G A A T
SEQ. ID. NO. 42 C T A C C A G T G G A A G C G C G T G G G C A C G

SEQ. ID. NO. 44 A G C C G C A G G G A C A T C C T G C C G G A C T
SEQ. ID. NO. 42 C T G A C G C A A G A C G T T C A G A G G T T C T

FIG. 13b.

SUBSTITUTE SHEET (RULE 26)

95/III

SEQ. ID. NO. 44 A T G A G C T C A A G C T C A T C C A C C A C G A
SEQ. ID. NO. 42 C T G A G G T G C G G A A T G A C C T G A C T G G

SEQ. ID. NO. 44 C A G C A A G T G T G A T C C A G G C C A A G C C
SEQ. ID. NO. 42 A G T T C T G T A T G G C G A G G A C A T T G A G

SEQ. ID. NO. 44 A C C A A G T A C C T A T A T G A G C T G C T C T
SEQ. ID. NO. 42 A T T T C A G A C A C C G A G A G C T T C T C C A

SEQ. ID. NO. 44 A C A A C G A C C C T A T C A A G A T C A T C C T
SEQ. ID. NO. 42 A C G A T C C C T G T A C C A G T G T C A A A A A

SEQ. ID. NO. 44 T A T G C C T G G C T G C A G C T C T G T C T C C
SEQ. ID. NO. 42 G C T G A A G G G G A A T G A T G T G C G G A T C

SEQ. ID. NO. 44 A C G C T G G T G G C T G A G G C T G C T A G G A
SEQ. ID. NO. 42 A T C C T T G G C C A G T T T G A C C A G A A T A

SEQ. ID. NO. 44 T G T G G A A C C T C A T T G T G C T T T C C T A
SEQ. ID. NO. 42 T G G C A G C A A A A G T G T T C T G T T G T G C

SEQ. ID. NO. 44 T G G C T C C A G C T C A C C A G C C C T G T C A
SEQ. ID. NO. 42 A T A C G A G G A G A A C A T G T A T G G T A G T

SEQ. ID. NO. 44 A A C C G G C A G C G T T T C C C C A C T T T C T
SEQ. ID. NO. 42 A A A T A T C A G T G G A T C A T T C C G G G C T

SEQ. ID. NO. 44 T C C G A A C G C A C C C A T C A G C C A C A C T
SEQ. ID. NO. 42 G G T A C G A G C C T T C T T G G T G G G A G C A

SEQ. ID. NO. 44 C C A C A A C C C T A C C C G C G T G A A A C T C
SEQ. ID. NO. 42 G G T G C A C A C G G A A G C C A A C T C A T C C

SEQ. ID. NO. 44 T T T G A A A A G T G G G G C T G G A A G A A G A
SEQ. ID. NO. 42 C G C T G C C T C C G G A A G A A T C T G C T T G

SEQ. ID. NO. 44 T T G C T A C C A T C C A G C A G A C C A C T G A
SEQ. ID. NO. 42 C T G C C A T G G A G G G C T A C A T T G G C G T

FIG. 13c.
SUBSTITUTE SHEET (RULE 26)

96/III

SEQ. ID. NO. 44 G G T C T T C A C T T C G A C T C T G G A C G A C
SEQ. ID. NO. 42 G G A T T T C G A G C C C C T G A G C T C C A A G

SEQ. ID. NO. 44 C T G G A G G A A C G A G T G A A G G A G G C T G
SEQ. ID. NO. 42 C A G A T C A A G A C C A T C T C A G G A A A G A

SEQ. ID. NO. 44 G A A T T G A G A T T A C T T T C C G C C A G A G
SEQ. ID. NO. 42 C T C C A C A G C A G T A T G A G A G A G A G T A

SEQ. ID. NO. 44 T T T C T T C T C A G A T C C A G C T G T G C C C
SEQ. ID. NO. 42 C A A C A A C A A G C G G T C A G G C G T G G G G

SEQ. ID. NO. 44 G T C A A A A A C C T G A A G C G C C A G G A T G
SEQ. ID. NO. 42 C C C A G C A A G T T C C A C G G G T A C G C C T

SEQ. ID. NO. 44 C C C G A A T C A T C G T G G G A C T T T T T C T A
SEQ. ID. NO. 42 A C G A T G G C A T C T G G G T C A T C G C C A A

SEQ. ID. NO. 44 T G A G A C T G A A G C C C G G A A A G T T T T T
SEQ. ID. NO. 42 G A C A C T G C A G A G G G C C A T G G A G A C A

SEQ. ID. NO. 44 T G T G A G G T G T A C A A G G A G C G T C T C T
SEQ. ID. NO. 42 C T G C A T G C C A G C A G C C G G C A C C A G C

SEQ. ID. NO. 44 T T G G G A A G A A G T A C G T C T G G T T C C T
SEQ. ID. NO. 42 G G A T C C A G G A C T T C A A C T A C A C G G A

SEQ. ID. NO. 44 C A T T G G G T G G T A T G C T G A C A A T T G G
SEQ. ID. NO. 42 C C A C A C G C T G G G C A G G A T C A T C C T C

SEQ. ID. NO. 44 T T C A A G A T C T A C G A C C C T T C T A T C A
SEQ. ID. NO. 42 A A T G C C A T G A A C G A G A C C A A C T T C T

SEQ. ID. NO. 44 A C T G C A C A G T G G A T G A G A T G A C T G A
SEQ. ID. NO. 42 T C G G G G T C A C G G G T C A A G T T G T A T T

SEQ. ID. NO. 44 G G C G G T G G A G G G C C A C A T C A C A A C T
SEQ. ID. NO. 42 C C G G A A T G G G G A G A G A A T G G G G A C C

FIG. 13d.

SUBSTITUTE SHEET (RULE 26)

97/III

SEQ. ID. NO. 44 G A G A T T G T C A T G C T G A A T C C T G C C A
SEQ. ID. NO. 42 A T T A A A T T T A C T C A A T T T C A A G A C A

SEQ. ID. NO. 44 A T A C C C G C A G C A T T T C C A A C A T G A C
SEQ. ID. NO. 42 G C A G G G A G G T G A A G G T G G G A G A G T A

SEQ. ID. NO. 44 A T C C C A G G A A T T T G T G G A G A A A C T A
SEQ. ID. NO. 42 C A A C G C T G T G G C C G A C A C A C T G G A G

SEQ. ID. NO. 44 A C C A A G C G A C T G A A A A G A C A C C C T G
SEQ. ID. NO. 42 A T C A T C A A T G A C A C C A T C A G G T T C C

SEQ. ID. NO. 44 A G G A G A C A G G A G G C T T C C A G G A G G C
SEQ. ID. NO. 42 A A G G A T C C G A A C C A C C A A A A G A C A A

SEQ. ID. NO. 44 A C C G C T G G C C T A T G A T G C C A T C T G G
SEQ. ID. NO. 42 G A C C A T C A T C C T G G A G C A G C T G C G G

SEQ. ID. NO. 44 G C C T T G G C A C T G G C C C T G A A C A A G A
SEQ. ID. NO. 42 A A G A T C T C C C T A C C T C T C T A C A G C A

SEQ. ID. NO. 44 C A T C T G G A G G A G G C G G C C G T T C T G G
SEQ. ID. NO. 42 T C C T C T C T G C C C T C A C C A T C C T C G G

SEQ. ID. NO. 44 T G T G C G C C T G G A G G A C T T C A A C T A C
SEQ. ID. NO. 42 G A T G A T C A T G G C C A G T G C T T T T C T C

SEQ. ID. NO. 44 A A C A A C C A G A C C A T T A C C G A C C A A A
SEQ. ID. NO. 42 T T C T T C A A C A T C A A G A A C C G G A A T C

SEQ. ID. NO. 44 T C T A C C G G G C A A T G A A C T C T T C G T C
SEQ. ID. NO. 42 A G A A G C T C A T A A A G A T G T C G A G T C C

SEQ. ID. NO. 44 C T T T G A G G G T G T C T C T G G C C A T G T G
SEQ. ID. NO. 42 A T A C A T G A A C A A C C T T A T C A T C C T T

SEQ. ID. NO. 44 G T G T T T G A T G C C A G C G G C T C T C G G A
SEQ. ID. NO. 42 G G A G G G A T G C T C T C C T A T G C T T C C A

FIG. 13e.
SUBSTITUTE SHEET (RULE 26)

98/III

SEQ. ID. NO. 44 T G G C A T G G A C G C T T A T C G A G C A G C T
SEQ. ID. NO. 42 T A T T T C T C T T T G G C C T T G A T G G A T C

SEQ. ID. NO. 44 T C A G G G T G G C A G C T A C A A G A A G A T T
SEQ. ID. NO. 42 C T T T G T C T C T G A A A A G A C C T T T G A A

SEQ. ID. NO. 44 G G C T A C T A T G A C A G C A C C A A G G A T G
SEQ. ID. NO. 42 A C A C T T T G C A C C G T C A G G A C C T G G A

SEQ. ID. NO. 44 A T C T T T C C T G G T C C A A A A C A G A T A A
SEQ. ID. NO. 42 T T C T C A C C G T G G G C T A C A C G A C C G C

SEQ. ID. NO. 44 A T G G A T T G G A G G G T C C C C C C A G C T
SEQ. ID. NO. 42 T T T T G G G G C C A T G T T T G C A A A G A C C

SEQ. ID. NO. 44 G A C C A G A C C C T G G T C A T C A A G A C A T
SEQ. ID. NO. 42 T G G A G A G T C C A C G C C A T C T T C A A A A

SEQ. ID. NO. 44 T C C G C T T C C T G T C A C A G A A A C T C T T
SEQ. ID. NO. 42 A T G T G A A A A T G A A G A A G A A G A T C A T

SEQ. ID. NO. 44 T A T C T C C G T C T C A G T T C T C T C C A G C
SEQ. ID. NO. 42 C A A G G A C C A G A A A C T G C T T G T G A T C

SEQ. ID. NO. 44 C T G G G C A T T G T C C T A G C T G T T G T C T
SEQ. ID. NO. 42 G T G G G G G G C A T G C T G C T G A T C G A C C

SEQ. ID. NO. 44 G T C T G T C C T T T A A C A T C T A C A A C T C
SEQ. ID. NO. 42 T G T G T A T C C T G A T C T G C T G G C A G G C

SEQ. ID. NO. 44 A C A T G T C C G T T A T A T C C A G A A C T C A
SEQ. ID. NO. 42 T G T G G A C C C C C T G C G A A G G A C A G T G

SEQ. ID. NO. 44 C A G C C C A A C C T G A A C A A C C T G A C T G
SEQ. ID. NO. 42 G A G A A G T A C A G C A T G G A G C C G G A C C

SEQ. ID. NO. 44 C T G T G G G C T G C T C A C T G G C T T T A G C
SEQ. ID. NO. 42 C A G C A G G A C G G G A T A T C T C C A T C C G

FIG. 13f.
SUBSTITUTE SHEET (RULE 26)

99/III

SEQ. ID. NO. 44 T G C T G T C T T C C C C C T G G G G C T C G A T
SEQ. ID. NO. 42 C C C T C T C C T G G A G C A C T G T G A G A A C

SEQ. ID. NO. 44 G G T T A C C A C A T T G G G A G G A A C C A G T
SEQ. ID. NO. 42 A C C C A T A T G A C C A T C T G G C T T G G C A

SEQ. ID. NO. 44 T T C C T T T C G T C T G C C A G G C C C G C C T
SEQ. ID. NO. 42 T C G T C T A T G C C T A C A A G G G A C T T C T

SEQ. ID. NO. 44 C T G G C T C C T G G G C C T G G G C T T T A G T
SEQ. ID. NO. 42 C A T G T T G T T C G G T T G T T T C T T A G C T

SEQ. ID. NO. 44 C T G G G C T A C G G T T C C A T G T T C A C C A
SEQ. ID. NO. 42 T G G G A G A C C C G C A A C G T C A G C A T C C

SEQ. ID. NO. 44 A G A T T T G G T G G G T C C A C A C G G T C T T
SEQ. ID. NO. 42 C C G C A C T C A A C G A C A G C A A G T A C A T

SEQ. ID. NO. 44 C A C A A A G A A G G A A G A A A A G A A G G A G
SEQ. ID. NO. 42 C G G G A T G A G T G T C T A C A A C G T G G G G

SEQ. ID. NO. 44 T G G A G G A A G A C T C T G G A A C C C T G G A
SEQ. ID. NO. 42 A T C A T G T G C A T C A T C G G G G C C G C T G

SEQ. ID. NO. 44 A G C T G T A T G C C A C A G T G G G C C T G C T
SEQ. ID. NO. 42 T C T C C T T C C T G A C C C G G G A C C A G C C

SEQ. ID. NO. 44 G G T G G G C A T G G A T G T C C T C A C T C T C
SEQ. ID. NO. 42 C A A T G T G C A G T T C T G C A T C G T G G C T

SEQ. ID. NO. 44 G C C A T C T G G C A G A T C G T G G A C C C T C
SEQ. ID. NO. 42 C T G G T C A T C A T C T T C T G C A G C A C C A

SEQ. ID. NO. 44 T G C A C C G G A C C A T T G A G A C A T T T T G C
SEQ. ID. NO. 42 T C A C C C T C T G C C T G G T A T T C G T G C C

SEQ. ID. NO. 44 C A A G G A G G A A C C T A A G G A A G A T A T T
SEQ. ID. NO. 42 G A A G C T C A T C A C C C T G A G A A C A A A C

FIG. 13g.

SUBSTITUTE SHEET (RULE 26)

100/111

SEQ. ID. NO. 44 G A C G T C T C T A T T C T G C C C C A G C T G G
SEQ. ID. NO. 42 C C A G A T G C A G C A A C G C A G A A C A G G C

SEQ. ID. NO. 44 A G C A T T G C A G C T C C A G G A A G A T G A A
SEQ. ID. NO. 42 G A T T C C A G T T C A C T C A G A A T C A G A A

SEQ. ID. NO. 44 T A C A T G G C T T G G C A T T T T C T A T G G T
SEQ. ID. NO. 42 G A A A G A A G A T T C T A A A A C G T C C A C C

SEQ. ID. NO. 44 T A C A A G G G G C T G C T G C T G C T G C T G G
SEQ. ID. NO. 42 T C G G T C A C C A G T G T G A A C C A A G C C A

SEQ. ID. NO. 44 G A A T C T T C C T T G C T T A T G A G A C C A A
SEQ. ID. NO. 42 G C A C A T C C C G C C T G G A G G G C C T A C A

SEQ. ID. NO. 44 G A G T G T G T C C A C T G A G A A G A T C A A T
SEQ. ID. NO. 42 G T C A G A A A A C C A T C G C C T G C G A A T G

SEQ. ID. NO. 44 G A T C A C C G G G C T G T G G G C A T G G C T A
SEQ. ID. NO. 42 A A G A T C A C A G A G C T G G A T A A A G A C T

SEQ. ID. NO. 44 T C T A C A A T G T G G C A G T C C T G T G C C T
SEQ. ID. NO. 42 T G G A A G A G G T C A C C A T G C A G C T G C A

SEQ. ID. NO. 44 C A T C A C T G C T C C T G T C A C C A T G A T T
SEQ. ID. NO. 42 G G A C A C A C C A G A A A A G A C C A C C T A C

SEQ. ID. NO. 44 C T G T C C A G C C A G C A G G A T G C A G C C T
SEQ. ID. NO. 42 A T T A A A C A G A A C C A C T A C C A A G A G C

SEQ. ID. NO. 44 T T G C C T T T G C C T C T C T T G C C A T A G T
SEQ. ID. NO. 42 T C A A T G A C A T C C T C A A C C T G G G A A A

SEQ. ID. NO. 44 T T T C T C C T C C T A T A T C A C T C T T G T T
SEQ. ID. NO. 42 C T T C A C T G A G A G C A C A G A T G G A G G A

SEQ. ID. NO. 44 G T G C T C T T T G T G C C C A A G A T G C G C A
SEQ. ID. NO. 42 A A G G C C A T T T T A A A A A A T C A C C T C G

FIG. 13h.

SUBSTITUTE SHEET (RULE 26)

101/III

SEQ. ID. NO. 44 G G C T G A T C A C C C G A G G G G A A T G G C A
SEQ. ID. NO. 42 A T C A A A A T C C C C A G C T A C A G T G G A A

SEQ. ID. NO. 44 G T C G G A G G C G C A G G A C A C C A T G A A G
SEQ. ID. NO. 42 C A C A A C A G A G C C C T C T C G A A C A T G C

SEQ. ID. NO. 44 A C A G G G T C A T C G A C C A A C A A C A A C G
SEQ. ID. NO. 42 A A A G A T C C T A T A G A A G A T A T A A A C T

SEQ. ID. NO. 44 A G G A G G A G A A G T C C C G G C T G T T G G A
SEQ. ID. NO. 42 C T C C A G A A C A C A T C C A G C G T C G G C T

SEQ. ID. NO. 44 G A A G G A G A A C C G T G A A C T G G A A A A G
SEQ. ID. NO. 42 G T C C C T C C A G C T C C C C A T C C T C C A C

SEQ. ID. NO. 44 A T C A T T G C T G A G A A A G A G G A G C G T G
SEQ. ID. NO. 42 C A C G C C T A C C T C C C A T C C A T C G G A G

SEQ. ID. NO. 44 T C T C T G A A C T G C G C C A T C A A C T C C A
SEQ. ID. NO. 42 G C G T G G A C G C C A G C T G T G T C A G C C C

SEQ. ID. NO. 44 G T C T C G G C A G C A G C T C C G C T C C C G G
SEQ. ID. NO. 42 C T G C G T C A G C C C C A C C G C C A G C C C C

SEQ. ID. NO. 44 C G C C A C C C A C C G A C A C C C C C A G A A C
SEQ. ID. NO. 42 C G C C A C A G A C A T G T G C C A C C C T C C T

SEQ. ID. NO. 44 C C T C T G G G G G C C T G C C C A G G G G A C C
SEQ. ID. NO. 42 T C C G A G T C A T G G T C T C G G G C C T G G C

SEQ. ID. NO. 44 C C C T G A G C C C C C C G A C C G G C T T A G C
SEQ. ID. NO. 42 G G C C G C C A T G A C T C T G G A G T C C A T C

SEQ. ID. NO. 44 T G T G A T G G G A G T C G A G T G C A T T T G C
SEQ. ID. NO. 42 A T G G C G T G C T G C C T G A G C G A G G A G G

SEQ. ID. NO. 44 T T T A T A A G G C G G C C G C C A T G A C T C T
SEQ. ID. NO. 42 C C A A G G A A G C C C G G C G G A T C A A C G A

FIG. 13i.

SUBSTITUTE SHEET (RULE 26)

102/III

SEQ. ID. NO. 44 G G A G T C C A T C A T G G C G T G C T G C C T G
SEQ. ID. NO. 42 C G A G A T C G A G C G G C A G C T C C G C A G G

SEQ. ID. NO. 44 A G C G A G G A G G C C A A G G A A G C C C G G C
SEQ. ID. NO. 42 G A C A A G C G G G A C G C C C G C C G G G A G C

SEQ. ID. NO. 44 G G A T C A A C G A C G A G A T C G A G C G G C A
SEQ. ID. NO. 42 T C A A G C T G C T G C T G C T C G G G A C A G G

SEQ. ID. NO. 44 G C T C C G C A G G G A C A A G C G G G A C G C C
SEQ. ID. NO. 42 A G A G A G T G G C A A G A G T A C G T T T A T C

SEQ. ID. NO. 44 C G C C G G G A G C T C A A G C T G C T G C T G C
SEQ. ID. NO. 42 A A G C A G A T G A G A A T C A T C C A T G G G T

SEQ. ID. NO. 44 T C G G G A C A G G A G A G A G T G G C A A G A G
SEQ. ID. NO. 42 C A G G A T A C T C T G A T G A A G A T A A A A G

SEQ. ID. NO. 44 T A C G T T T A T C A A G C A G A T G A G A A T C
SEQ. ID. NO. 42 G G G C T T C A C C A A G C T G G T G T A T C A G

SEQ. ID. NO. 44 A T C C A T G G G T C A G G A T A C T C T G A T G
SEQ. ID. NO. 42 A A C A T C T T C A C G G C C A T G C A G G C C A

SEQ. ID. NO. 44 A A G A T A A A A G G G G C T T C A C C A A G C T
SEQ. ID. NO. 42 T G A T C A G A G C C A T G G A C A C A C T C A A

SEQ. ID. NO. 44 G G T G T A T C A G A A C A T C T T C A C G G C C
SEQ. ID. NO. 42 G A T C C C A T A C A A G T A T G A G C A C A A T

SEQ. ID. NO. 44 A T G C A G G C C A T G A T C A G A G C C A T G G
SEQ. ID. NO. 42 A A G G C T C A T G C A C A A T T A G T T C G A G

SEQ. ID. NO. 44 A C A C A C T C A A G A T C C C A T A C A A G T A
SEQ. ID. NO. 42 A A G T T G A T G T G G A G A A G G T G T C T G C

SEQ. ID. NO. 44 T G A G C A C A A T A A G G C T C A T G C A C A A
SEQ. ID. NO. 42 T T T T G A G A A T C C A T A T G T A G A T G C A

FIG. 13j.

SUBSTITUTE SHEET (RULE 26)

103/III

SEQ. ID. NO. 44 T T A G T T C G A G A A G T T G A T G T G G A G A
SEQ. ID. NO. 42 A T A A A G A G T T T A T G G A A T G A T C C T G

SEQ. ID. NO. 44 A G G T G T C T G C T T T T G A G A A T C C A T A
SEQ. ID. NO. 42 G A A T C C A G G A A T G C T A T G A T A G A C G

SEQ. ID. NO. 44 T G T A G A T G C A A T A A A G A G T T T A T G G
SEQ. ID. NO. 42 A C G A G A A T A T C A A T T A T C T G A C T C T

SEQ. ID. NO. 44 A A T G A T C C T G G A A T C C A G G A A T G C T
SEQ. ID. NO. 42 A C C A A A T A C T A T C T T A A T G A C T T G G

SEQ. ID. NO. 44 A T G A T A G A C G A C G A G A A T A T C A A T T
SEQ. ID. NO. 42 A C C G C G T A G C T G A C C C T G C C T A C C T

SEQ. ID. NO. 44 A T C T G A C T C T A C C A A A T A C T A T C T T
SEQ. ID. NO. 42 G C C T A C G C A A C A A G A T G T G C T T A G A

SEQ. ID. NO. 44 A A T G A C T T G G A C C G C G T A G C T G A C C
SEQ. ID. NO. 42 G T T C G A G T C C C C A C C A C A G G G A T C A

SEQ. ID. NO. 44 C T G C C T A C C T G C C T A C G C A A C A A G A
SEQ. ID. NO. 42 T C G A A T A C C C C T T T G A C T T A C A A A G

SEQ. ID. NO. 44 T G T G C T T A G A G T T C G A G T C C C C A C C
SEQ. ID. NO. 42 T G T C A T T T T T C A G A A T G G T C G A T G T A

SEQ. ID. NO. 44 A C A G G G A T C A T C G A A T A C C C C T T T G
SEQ. ID. NO. 42 G G G G G C C A A A G G T C A G A G A G A A G A A

SEQ. ID. NO. 44 A C T T A C A A A G T G T C A T T T T T C A G A A T
SEQ. ID. NO. 42 A A T G G A T A C A C T G C T T T T G A A A A T G T

SEQ. ID. NO. 44 G G T C G A T G T A G G G G G C C A A A G G T C A
SEQ. ID. NO. 42 C A C C T C T A T C A T G T T T T C T A G T A G C G

SEQ. ID. NO. 44 G A G A G A A G A A A A T G G A T A C A C T G C T
SEQ. ID. NO. 42 C T T A G T G A A T A T G A T C A A G T T C T G G

FIG. 13k.

SUBSTITUTE SHEET (RULE 26)

104/III

SEQ. ID. NO. 44 TTGAA AATGTCACCTCTATCATGTT
SEQ. ID. NO. 42 TGGAGTTCAGACAATGAGAACCGAAT

SEQ. ID. NO. 44 TCTAGTAGCGCTTAGTGAAATATGAT
SEQ. ID. NO. 42 GGAGGAAAGCAAGGCTCTCTTTAGA

SEQ. ID. NO. 44 CAAGTTCTCTGTGGAGTCAGACAATG
SEQ. ID. NO. 42 ACAATTATCACATACCCCTGGTTCC

SEQ. ID. NO. 44 AGAACC GAATGGAGGAAAGCAAGGC
SEQ. ID. NO. 42 AGAACTCTCTCGGTTATTCTGTTCTT

SEQ. ID. NO. 44 TCTCTTTAGAACAAATTATCACATAC
SEQ. ID. NO. 42 AAACAAGAAAGATCTTCTAGAGGAG

SEQ. ID. NO. 44 CCCTGGTTTCCAGAACTCCTCGGTTA
SEQ. ID. NO. 42 AAAATCATGTATTCCCATCTAGTCG

SEQ. ID. NO. 44 TTCTGTTCTTAAACAAGAAAGATCT
SEQ. ID. NO. 42 ACTACTTCCCAGAAATATGATGGACC

SEQ. ID. NO. 44 TCTAGAGGAGAAAATCATGTATTCC
SEQ. ID. NO. 42 CCAGAGAGATGCCCAGGCAGCCCCGA

SEQ. ID. NO. 44 CATCTAGTCGACTACTTCCCAGAAAT
SEQ. ID. NO. 42 GAATTCAATTCTGAAGATGTTCTGTGG

SEQ. ID. NO. 44 ATGATGGACCC CAGAGAGATGCCCA
SEQ. ID. NO. 42 ACCTGAACCC CAGACAGTGACAAAAT

SEQ. ID. NO. 44 GGCAGCCCGAGAAATTCATTCTGAAG
SEQ. ID. NO. 42 TAACTACTCCC ACTTTCACGTGCGCC

SEQ. ID. NO. 44 ATGTTCTGTGGACCTGAACCCAGACA
SEQ. ID. NO. 42 ACAGACACCCGAGAAATATCCGCTTTG

SEQ. ID. NO. 44 GTGACAAAATTATCTACTCCC ACTT
SEQ. ID. NO. 42 TCTTTGCTGCCGTCAAAGGACACCAT

FIG. 13L

SUBSTITUTE SHEET (RULE 26)

105/III

SEQ. ID. NO. 44 C A C G T G C G C C A C A G A C A C C G A G A A T
SEQ. ID. NO. 42 C C T C C A G T T G A A C C T G A A G G G C T G C

SEQ. ID. NO. 44 A T C C G C T T T G T C T T T G C T G C C G T C A
SEQ. ID. NO. 42 G G T C T G T A C

SEQ. ID. NO. 44 A G G A C A C C A T C C T C C A G T T G A A C C T
SEQ. ID. NO. 42

SEQ. ID. NO. 44 G A A G G G C T G C G G T C T G T A C
SEQ. ID. NO. 42

FIG. 13m.

106/III

ClustalW Formatted Alignments

SEQ. ID. NO. 45 M L L L L L L A P L F L R P P G A G G A Q T P N A
SEQ. ID. NO. 43 M A S P R S S G Q P G P P P P P P P P A R L L L

SEQ. ID. NO. 45 T S E G C Q I I H P P W E G G I R Y R G L T R D Q
SEQ. ID. NO. 43 L L L L P L L L P L A P G A W G W A R G A P R P P

SEQ. ID. NO. 45 V K A I N F L P V D Y E I E Y V C R G E R E V V G
SEQ. ID. NO. 43 P S S P P L S I M G L M P L T K E V A K G S I G R

SEQ. ID. NO. 45 P K V R K C L A N G S W T D M D T P S R C V R I C
SEQ. ID. NO. 43 G V L P A V E L A I E Q I R N E S L L R P Y F L D

SEQ. ID. NO. 45 S K S Y L T L E N G K V F L T G G D L P A L D G A
SEQ. ID. NO. 43 L R L Y D T E C D N A K G L K A F Y D A I K Y G P

SEQ. ID. NO. 45 R V D F R C D P D F H L V G S S R S I C S Q G Q W
SEQ. ID. NO. 43 N H L M V F G G V C P S V T S I I A E S L Q G W N

SEQ. ID. NO. 45 S T P K P H C Q V N R T P H S E R R A V Y I G A L
SEQ. ID. NO. 43 L V Q L S F A A T T P V L A D K K K Y P Y F F R T

SEQ. ID. NO. 45 F P M S G G W P G G Q A C Q P A V E M A L E D V N
SEQ. ID. NO. 43 V P S D N A V N P A I L K L L K H Y Q W K R V G T

SEQ. ID. NO. 45 S R R D I L P D Y E L K L I H H D S K C D P G Q A
SEQ. ID. NO. 43 L T Q D V Q R F S E V R N D L T G V L Y G E D I E

SEQ. ID. NO. 45 T K Y L Y E L L Y N D P I K I I L M P G C S S V S
SEQ. ID. NO. 43 I S D T E S F S N D P C T S V K K L K G N D V R I

SEQ. ID. NO. 45 T L V A E A A R M W N L I V L S Y G S S S P A L S
SEQ. ID. NO. 43 I L G Q F D Q N M A A K V F C C A Y E E N M Y G S

SEQ. ID. NO. 45 N R Q R F P T F F R T H P S A T L H N P T R V K L
SEQ. ID. NO. 43 K Y Q W I I P G W Y E P S W W E Q V H T E A N S S

FIG. 14a.

107/III

SEQ. ID. NO. 45 FEK WGWKKIATIQQTTTEVFTSTLDD
 SEQ. ID. NO. 43 RCLRKNNLLAAMEGYIGVDFEPLSSK

SEQ. ID. NO. 45 LEERVKEAGIEITFRQSFFSDPAVP
 SEQ. ID. NO. 43 QIKTISGKTPQQYEREYNNKRSGVG

SEQ. ID. NO. 45 VKNLKRQDARIIVGLFYETEARKVVF
 SEQ. ID. NO. 43 PSKFHGYAYDGIWVIAKTLQRAMET

SEQ. ID. NO. 45 CEVYKERLFGKKYVWFLIGWYADNW
 SEQ. ID. NO. 43 LHASSRHQRIQDFNYTDHTLGRIL

SEQ. ID. NO. 45 FKIYDPSINCTVDEMTEAVEGHITT
 SEQ. ID. NO. 43 NAMNETNFFGVGTGQVVFRNGERMGT

SEQ. ID. NO. 45 EIVMLNPANTRSISNMTSQEFVEKL
 SEQ. ID. NO. 43 IKFTQFQDSREVKVGEYNAVADTLE

SEQ. ID. NO. 45 TKRLKRHPREETGG - FQEAPLAYDAI
 SEQ. ID. NO. 43 IINDTIRFQGSEPPKDKTIILEQLR

SEQ. ID. NO. 45 WALALALNKTSGGGGRSGVRLDFN
 SEQ. ID. NO. 43 KISLPLYSILSALTILGMIMASAFLL

SEQ. ID. NO. 45 YNNQTITDQIYRAMNSSSSFEGVSGH
 SEQ. ID. NO. 43 FFNIKNRNQKLIKMSSPYMNNLIIL

SEQ. ID. NO. 45 VVFDASGSRMAWTLIEQLQGGSYKK
 SEQ. ID. NO. 43 GGMLSYSASIFLFGLDGSFVSEKTFE

SEQ. ID. NO. 45 IGYDSTKDDL SWSKTDKWIGGSPP
 SEQ. ID. NO. 43 TLCTVRTWILTVGYTTAFGAMFAKT

SEQ. ID. NO. 45 ADQTLVIKTRFLSQKLFISVSVLS
 SEQ. ID. NO. 43 WRVHAIFKNVKMKKKIKDKQLLVI

SEQ. ID. NO. 45 SLGIVLAVVCLSFNIYN SHVRYIQN
 SEQ. ID. NO. 43 VGGMLLIDLCLICWQAVDPLRRTV

FIG. 14b.

108/III

SEQ. ID. NO. 45 S Q P N L N N L T A V G C S L A L A A V F P L G L
 SEQ. ID. NO. 43 E K Y S M E P D P A G R D I S I R P L L E H C E N

SEQ. ID. NO. 45 D G Y H I G R N Q F P F V C Q A R L W L L G L G F
 SEQ. ID. NO. 43 T H M T I W L G I V Y A Y K G L L M L F G C F L A

SEQ. ID. NO. 45 S L G Y G S M F T K I W W V H T V F T K K E E K K
 SEQ. ID. NO. 43 W E T R N V S I P A L N D S K Y I G M S V Y N V G

SEQ. ID. NO. 45 E W R K T L E P W K L Y A T V G L L V G M D V L T
 SEQ. ID. NO. 43 I M C I I G A A V S F L T R D Q P N V Q F C I V A

SEQ. ID. NO. 45 L A I W Q I V D P L H R T I E T F A K E E P K E D
 SEQ. ID. NO. 43 L V I I F C S T I T L C L V F V P K L I T L R T N

SEQ. ID. NO. 45 I D V S I L P Q L E H C S S R K M N T W L G I F Y
 SEQ. ID. NO. 43 P D A A T Q N R R F Q F T Q N Q K K E D S K T S T

SEQ. ID. NO. 45 G Y K G L L L L L G I F L A Y E T K S V S T E K I
 SEQ. ID. NO. 43 S V T S V N Q A S T S R L E G L Q S E N H R L R M

SEQ. ID. NO. 45 N D H R A V G M A I Y N V A V L C L I T A P V T M
 SEQ. ID. NO. 43 K I T E L D K D L E E V T M Q L Q D T P E K T T Y

SEQ. ID. NO. 45 I L S S Q Q D A A F A F A S L A I V F S S Y I T L
 SEQ. ID. NO. 43 I K Q N H Y Q E L N D I L N L G N F T E S T D G G

SEQ. ID. NO. 45 V V L F V P K M R R L I T R G E W Q S E A Q D T M
 SEQ. ID. NO. 43 K A I L K N H L D Q N P Q L Q W N T T E P S R T C

SEQ. ID. NO. 45 K T G S S T N N N E E E K S R L L E K E N R E L E
 SEQ. ID. NO. 43 K D P I E D I N S P E H I Q R R L S L Q L P I L H

SEQ. ID. NO. 45 K I I A E K E E R V S E L R H Q L Q S R Q Q L R S
 SEQ. ID. NO. 43 H A Y L P S I G G V D A S C V S P C V S P T A S P

SEQ. ID. NO. 45 R R H P P T P P E P S G G L P R G P P E P P D R L
 SEQ. ID. NO. 43 R H R H V P P S F R V M V S G L A A A M T L E S I

FIG. 14c.

SUBSTITUTE SHEET (RULE 26)

109/III

SEQ. ID. NO. 45 S C D G S R V H L L Y K A A A M T L E S I M A C C
 SEQ. ID. NO. 43 M A C C L S E E A K E A R R I N D E I E R Q L R R

SEQ. ID. NO. 45 L S E E A K E A R R I N D E I E R Q L R R D K R D
 SEQ. ID. NO. 43 D K R D A R R E L K L L L L G T G E S G K S T F I

SEQ. ID. NO. 45 A R R E L K L L L L G T G E S G K S T F I K Q M R
 SEQ. ID. NO. 43 K Q M R I I H G S G Y S D E D K R G F T K L V Y Q

SEQ. ID. NO. 45 I I H G S G Y S D E D K R G F T K L V Y Q N I F T
 SEQ. ID. NO. 43 N I F T A M Q A M I R A M D T L K I P Y K Y E H N

SEQ. ID. NO. 45 A M Q A M I R A M D T L K I P Y K Y E H N K A H A
 SEQ. ID. NO. 43 K A H A Q L V R E V D V E K V S A F E N P Y V D A

SEQ. ID. NO. 45 Q L V R E V D V E K V S A F E N P Y V D A I K S L
 SEQ. ID. NO. 43 I K S L W N D P G I Q E C Y D R R R E Y Q L S D S

SEQ. ID. NO. 45 W N D P G I Q E C Y D R R R E Y Q L S D S T K Y Y
 SEQ. ID. NO. 43 T K Y Y L N D L D R V A D P A Y L P T Q Q D V L R

SEQ. ID. NO. 45 L N D L D R V A D P A Y L P T Q Q D V L R V R V P
 SEQ. ID. NO. 43 V R V P T T G I I E Y P F D L Q S V I F R M V D V

SEQ. ID. NO. 45 T T G I I E Y P F D L Q S V I F R M V D V G G Q R
 SEQ. ID. NO. 43 G G Q R S E R R K W I H C F E N V T S I M F L V A

SEQ. ID. NO. 45 S E R R K W I H C F E N V T S I M F L V A L S E Y
 SEQ. ID. NO. 43 L S E Y D Q V L V E S D N E N R M E E S K A L F R

SEQ. ID. NO. 45 D Q V L V E S D N E N R M E E S K A L F R T I I T
 SEQ. ID. NO. 43 T I I T Y P W F Q N S S V I L F L N K K D L L E E

SEQ. ID. NO. 45 Y P W F Q N S S V I L F L N K K D L L E E K I M Y
 SEQ. ID. NO. 43 K I M Y S H L V D Y F P E Y D G P Q R D A Q A A R

SEQ. ID. NO. 45 S H L V D Y F P E Y D G P Q R D A Q A A R E F I L
 SEQ. ID. NO. 43 E F I L K M F V D L N P D S D K I N Y S H F T C A

FIG. 14d.

SUBSTITUTE SHEET (RULE 26)

110/111

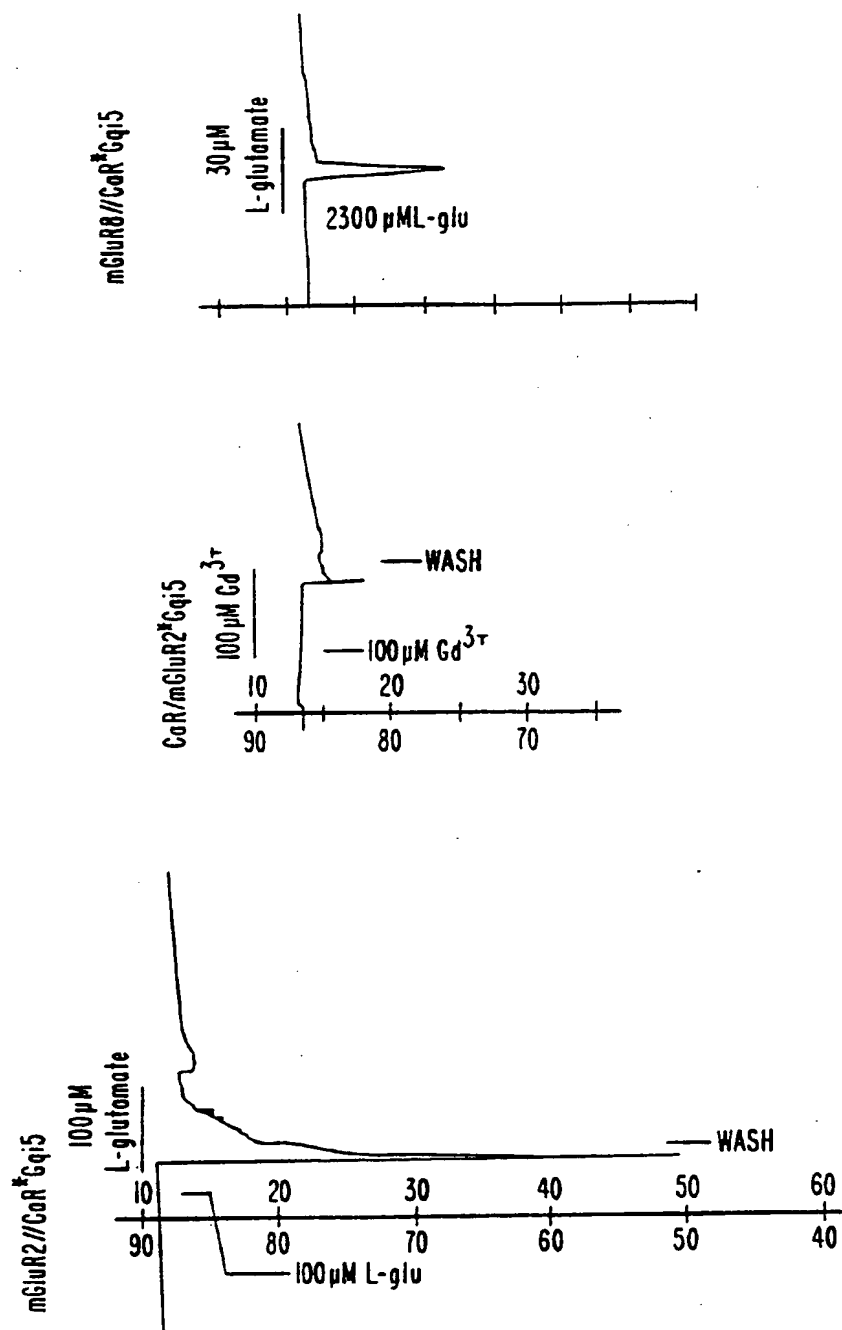
SEQ. ID. NO. 45 K M F V D L N P D S D K I I Y S H F T C A T D T E
SEQ. ID. NO. 43 T D T E N I R F V F A A V K D T I L Q L N L K G C

SEQ. ID. NO. 45 N I R F V F A A V K D T I L Q L N L K G C G L Y
SEQ. ID. NO. 43 G L Y

FIG. 14e.

III/III

FIG. 15.



SUBSTITUTE SHEET (RULE 26)

SEQUENCE LISTING

<110> NPS PHARMACEUTICALS, INC.

<120> G-PROTEIN FUSION RECEPTORS AND CHIMERIC
GABA_B RECEPTORS

<130> 241/086-PCT

<140> TO BE ASSIGNED

<141> HEREWITH

<150> US 60/080,671

<151> 1998-04-03

<160> 47

<170> FastSEQ for Windows Version 3.0

<210> 1

<211> 612

<212> PRT

<213> Human

<400> 1

Met	Ala	Phe	Tyr	Ser	Cys	Cys	Trp	Val	Leu	Leu	Ala	Leu	Thr	Trp	His
1				5					10					15	
Thr	Ser	Ala	Tyr	Gly	Pro	Asp	Gln	Arg	Ala	Gln	Lys	Lys	Gly	Asp	Ile
			20					25					30		
Ile	Leu	Gly	Gly	Leu	Phe	Pro	Ile	His	Phe	Gly	Val	Ala	Ala	Lys	Asp
		35					40					45			
Gln	Asp	Leu	Lys	Ser	Arg	Pro	Glu	Ser	Val	Glu	Cys	Ile	Arg	Tyr	Asn
	50					55					60				
Phe	Arg	Gly	Phe	Arg	Trp	Leu	Gln	Ala	Met	Ile	Phe	Ala	Ile	Glu	Glu
65					70					75				80	
Ile	Asn	Ser	Ser	Pro	Ala	Leu	Leu	Pro	Asn	Leu	Thr	Leu	Gly	Tyr	Arg
				85					90					95	
Ile	Phe	Asp	Thr	Cys	Asn	Thr	Val	Ser	Lys	Ala	Leu	Glu	Ala	Thr	Leu
			100					105						110	

Ser Phe Val Ala Gln Asn Lys Ile Asp Ser Leu Asn Leu Asp Glu Phe
 115 120 125
 Cys Asn Cys Ser Glu His Ile Pro Ser Thr Ile Ala Val Val Gly Ala
 130 135 140
 Thr Gly Ser Gly Val Ser Thr Ala Val Ala Asn Leu Leu Gly Leu Phe
 145 150 155 160
 Tyr Ile Pro Gln Val Ser Tyr Ala Ser Ser Arg Leu Leu Ser Asn
 165 170 175
 Lys Asn Gln Phe Lys Ser Phe Leu Arg Thr Ile Pro Asn Asp Glu His
 180 185 190
 Gln Ala Thr Ala Met Ala Asp Ile Ile Glu Tyr Phe Arg Trp Asn Trp
 195 200 205
 Val Gly Thr Ile Ala Ala Asp Asp Asp Tyr Gly Arg Pro Gly Ile Glu
 210 215 220
 Lys Phe Arg Glu Glu Ala Glu Glu Arg Asp Ile Cys Ile Asp Phe Ser
 225 230 235 240
 Glu Leu Ile Ser Gln Tyr Ser Asp Glu Glu Glu Ile Gln His Val Val
 245 250 255
 Glu Val Ile Gln Asn Ser Thr Ala Lys Val Ile Val Val Phe Ser Ser
 260 265 270
 Gly Pro Asp Leu Glu Pro Leu Ile Lys Glu Ile Val Arg Arg Asn Ile
 275 280 285
 Thr Gly Lys Ile Trp Leu Ala Ser Glu Ala Trp Ala Ser Ser Ser Leu
 290 295 300
 Ile Ala Met Pro Gln Tyr Phe His Val Val Gly Gly Thr Ile Gly Phe
 305 310 315 320
 Ala Leu Lys Ala Gly Gln Ile Pro Gly Phe Arg Glu Phe Leu Lys Lys
 325 330 335
 Val His Pro Arg Lys Ser Val His Asn Gly Phe Ala Lys Glu Phe Trp
 340 345 350
 Glu Glu Thr Phe Asn Cys His Leu Gln Glu Gly Ala Lys Gly Pro Leu
 355 360 365
 Pro Val Asp Thr Phe Leu Arg Gly His Glu Glu Ser Gly Asp Arg Phe
 370 375 380
 Ser Asn Ser Ser Thr Ala Phe Arg Pro Leu Cys Thr Gly Asp Glu Asn
 385 390 395 400

3

Ile Ser Ser Val Glu Thr Pro Tyr Ile Asp Tyr Thr His Leu Arg Ile
 405 410 415
 Ser Tyr Asn Val Tyr Leu Ala Val Tyr Ser Ile Ala His Ala Leu Gln
 420 425 430
 Asp Ile Tyr Thr Cys Leu Pro Gly Arg Gly Leu Phe Thr Asn Gly Ser
 435 440 445
 Cys Ala Asp Ile Lys Lys Val Glu Ala Trp Gln Val Leu Lys His Leu
 450 455 460
 Arg His Leu Asn Phe Thr Asn Asn Met Gly Glu Gln Val Thr Phe Asp
 465 470 475 480
 Glu Cys Gly Asp Leu Val Gly Asn Tyr Ser Ile Ile Asn Trp His Leu
 485 490 495
 Ser Pro Glu Asp Gly Ser Ile Val Phe Lys Glu Val Gly Tyr Tyr Asn
 500 505 510
 Val Tyr Ala Lys Lys Gly Glu Arg Leu Phe Ile Asn Glu Glu Lys Ile
 515 520 525
 Leu Trp Ser Gly Phe Ser Arg Glu Val Pro Phe Ser Asn Cys Ser Arg
 530 535 540
 Asp Cys Leu Ala Gly Thr Arg Lys Gly Ile Ile Glu Gly Glu Pro Thr
 545 550 555 560
 Cys Cys Phe Glu Cys Val Glu Cys Pro Asp Gly Glu Tyr Ser Asp Glu
 565 570 575
 Thr Asp Ala Ser Ala Cys Asn Lys Cys Pro Asp Asp Phe Trp Ser Asn
 580 585 590
 Glu Asn His Thr Ser Cys Ile Ala Lys Glu Ile Glu Phe Leu Ser Trp
 595 600 605
 Thr Glu Pro Phe
 610

<210> 2
 <211> 590
 <212> PRT
 <213> Human

<400> 2

Met Leu Leu Leu Leu Leu Leu Ala Pro Leu Phe Leu Arg Pro Pro Gly
 1 5 10 15

Ala Gly Gly Ala Gln Thr Pro Asn Ala Thr Ser Glu Gly Cys Gln Ile
 20 25 30
 Ile His Pro Pro Trp Glu Gly Gly Ile Arg Tyr Arg Gly Leu Thr Arg
 35 40 45
 Asp Gln Val Lys Ala Ile Asn Phe Leu Pro Val Asp Tyr Glu Ile Glu
 50 55 60
 Tyr Val Cys Arg Gly Glu Arg Glu Val Val Gly Pro Lys Val Arg Lys
 65 70 75 80
 Cys Leu Ala Asn Gly Ser Trp Thr Asp Met Asp Thr Pro Ser Arg Cys
 85 90 95
 Val Arg Ile Cys Ser Lys Ser Tyr Leu Thr Leu Glu Asn Gly Lys Val
 100 105 110
 Phe Leu Thr Gly Gly Asp Leu Pro Ala Leu Asp Gly Ala Arg Val Asp
 115 120 125
 Phe Arg Cys Asp Pro Asp Phe His Leu Val Gly Ser Ser Arg Ser Ile
 130 135 140
 Cys Ser Gln Gly Gln Trp Ser Thr Pro Lys Pro His Cys Gln Val Asn
 145 150 155 160
 Arg Thr Pro His Ser Glu Arg Arg Ala Val Tyr Ile Gly Ala Leu Phe
 165 170 175
 Pro Met Ser Gly Gly Trp Pro Gly Gly Gln Ala Cys Gln Pro Ala Val
 180 185 190
 Glu Met Ala Leu Glu Asp Val Asn Ser Arg Arg Asp Ile Leu Pro Asp
 195 200 205
 Tyr Glu Leu Lys Leu Ile His His Asp Ser Lys Cys Asp Pro Gly Gln
 210 215 220
 Ala Thr Lys Tyr Leu Tyr Glu Leu Leu Tyr Asn Asp Pro Ile Lys Ile
 225 230 235 240
 Ile Leu Met Pro Gly Cys Ser Ser Val Ser Thr Leu Val Ala Glu Ala
 245 250 255
 Ala Arg Met Trp Asn Leu Ile Val Leu Ser Tyr Gly Ser Ser Ser Pro
 260 265 270
 Ala Leu Ser Asn Arg Gln Arg Phe Pro Thr Phe Phe Arg Thr His Pro
 275 280 285
 Ser Ala Thr Leu His Asn Pro Thr Arg Val Lys Leu Phe Glu Lys Trp
 290 295 300

Gly Trp Lys Lys Ile Ala Thr Ile Gln Gln Thr Thr Glu Val Phe Thr
 305 310 315 320
 Ser Thr Leu Asp Asp Leu Glu Glu Arg Val Lys Glu Ala Gly Ile Glu
 325 330 335
 Ile Thr Phe Arg Gln Ser Phe Phe Ser Asp Pro Ala Val Pro Val Lys
 340 345 350
 Asn Leu Lys Arg Gln Asp Ala Arg Ile Ile Val Gly Leu Phe Tyr Glu
 355 360 365
 Thr Glu Ala Arg Lys Val Phe Cys Glu Val Tyr Lys Glu Arg Leu Phe
 370 375 380
 Gly Lys Lys Tyr Val Trp Phe Leu Ile Gly Trp Tyr Ala Asp Asn Trp
 385 390 395 400
 Phe Lys Ile Tyr Asp Pro Ser Ile Asn Cys Thr Val Asp Glu Met Thr
 405 410 415
 Glu Ala Val Glu Gly His Ile Thr Thr Glu Ile Val Met Leu Asn Pro
 420 425 430
 Ala Asn Thr Arg Ser Ile Ser Asn Met Thr Ser Gln Glu Phe Val Glu
 435 440 445
 Lys Leu Thr Lys Arg Leu Lys Arg His Pro Glu Glu Thr Gly Gly Phe
 450 455 460
 Gln Glu Ala Pro Leu Ala Tyr Asp Ala Ile Trp Ala Leu Ala Leu Ala
 465 470 475 480
 Leu Asn Lys Thr Ser Gly Gly Gly Gly Arg Ser Gly Val Arg Leu Glu
 485 490 495
 Asp Phe Asn Tyr Asn Asn Gln Thr Ile Thr Asp Gln Ile Tyr Arg Ala
 500 505 510
 Met Asn Ser Ser Ser Phe Glu Gly Val Ser Gly His Val Val Phe Asp
 515 520 525
 Ala Ser Gly Ser Arg Met Ala Trp Thr Leu Ile Glu Gln Leu Gln Gly
 530 535 540
 Gly Ser Tyr Lys Lys Ile Gly Tyr Tyr Asp Ser Thr Lys Asp Asp Leu
 545 550 555 560
 Ser Trp Ser Lys Thr Asp Lys Trp Ile Gly Gly Ser Pro Pro Ala Asp
 565 570 575
 Gln Thr Leu Val Ile Lys Thr Phe Arg Phe Leu Ser Gln Lys
 580 585 590

<210> 3
 <211> 473
 <212> PRT
 <213> Human

<400> 3

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Met Gly Pro Gly Ala Pro Phe Ala Arg Val Gly Trp Pro Leu Pro Leu
 1           5           10           15
Leu Val Val Met Ala Ala Gly Val Ala Pro Val Trp Ala Ser His Ser
      20           25           30
Pro His Leu Pro Arg Pro His Ser Arg Val Pro Pro His Pro Ser Ser
      35           40           45
Glu Arg Arg Ala Val Tyr Ile Gly Ala Leu Phe Pro Met Ser Gly Gly
      50           55           60
Trp Pro Gly Gly Gln Ala Cys Gln Pro Ala Val Glu Met Ala Leu Glu
      65           70           75           80
Asp Val Asn Ser Arg Arg Asp Ile Leu Pro Asp Tyr Glu Leu Lys Leu
      85           90           95
Ile His His Asp Ser Lys Cys Asp Pro Gly Gln Ala Thr Lys Tyr Leu
      100          105          110
Tyr Glu Leu Leu Tyr Asn Asp Pro Ile Lys Ile Ile Leu Met Pro Gly
      115          120          125
Cys Ser Ser Val Ser Thr Leu Val Ala Glu Ala Ala Arg Met Trp Asn
      130          135          140
Leu Ile Val Leu Ser Tyr Gly Ser Ser Ser Pro Ala Leu Ser Asn Arg
      145          150          155          160
Gln Arg Phe Pro Thr Phe Phe Arg Thr His Pro Ser Ala Thr Leu His
      165          170          175
Asn Pro Thr Arg Val Lys Leu Phe Glu Lys Trp Gly Trp Lys Lys Ile
      180          185          190
Ala Thr Ile Gln Gln Thr Thr Glu Val Phe Thr Ser Thr Leu Asp Asp
      195          200          205
Leu Glu Glu Arg Val Lys Glu Ala Gly Ile Glu Ile Thr Phe Arg Gln
      210          215          220
Ser Phe Phe Ser Asp Pro Ala Val Pro Val Lys Asn Leu Lys Arg Gln
      225          230          235          240
Asp Ala Arg Ile Ile Val Gly Leu Phe Tyr Glu Thr Glu Ala Arg Lys
      245          250          255

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7

Val Phe Cys Glu Val Tyr Lys Glu Arg Leu Phe Gly Lys Lys Tyr Val
 260 265 270
 Trp Phe Leu Ile Gly Trp Tyr Ala Asp Asn Trp Phe Lys Ile Tyr Asp
 275 280 285
 Pro Ser Ile Asn Cys Thr Val Asp Glu Met Thr Glu Ala Val Glu Gly
 290 295 300
 His Ile Thr Thr Glu Ile Val Met Leu Asn Pro Ala Asn Thr Arg Ser
 305 310 315 320
 Ile Ser Asn Met Thr Ser Gln Glu Phe Val Glu Lys Leu Thr Lys Arg
 325 330 335
 Leu Lys Arg His Pro Glu Glu Thr Gly Gly Phe Gln Glu Ala Pro Leu
 340 345 350
 Ala Tyr Asp Ala Ile Trp Ala Leu Ala Leu Ala Leu Asn Lys Thr Ser
 355 360 365
 Gly Gly Gly Gly Arg Ser Gly Val Arg Leu Glu Asp Phe Asn Tyr Asn
 370 375 380
 Asn Gln Thr Ile Thr Asp Gln Ile Tyr Arg Ala Met Asn Ser Ser Ser
 385 390 395 400
 Phe Glu Gly Val Ser Gly His Val Val Phe Asp Ala Ser Gly Ser Arg
 405 410 415
 Met Ala Trp Thr Leu Ile Glu Gln Leu Gln Gly Gly Ser Tyr Lys Lys
 420 425 430
 Ile Gly Tyr Tyr Asp Ser Thr Lys Asp Asp Leu Ser Trp Ser Lys Thr
 435 440 445
 Asp Lys Trp Ile Gly Gly Ser Pro Pro Ala Asp Gln Thr Leu Val Ile
 450 455 460
 Lys Thr Phe Arg Phe Leu Ser Gln Lys
 465 470

<210> 4
 <211> 480
 <212> PRT
 <213> Human

<400> 4

Met Ala Ser Pro Arg Ser Ser Gly Gln Pro Gly Pro Xaa Pro Pro Pro
 1 5 10 15

Pro Pro Pro Pro Ala Arg Leu Leu Leu Leu Leu Leu Leu Pro Leu Leu
 20 25 30
 Leu Pro Leu Ala Pro Gly Ala Trp Gly Trp Ala Arg Gly Ala Pro Arg
 35 40 45
 Pro Pro Pro Ser Ser Pro Pro Leu Ser Ile Met Gly Leu Met Pro Leu
 50 55 60
 Thr Lys Glu Val Ala Lys Gly Ser Ile Gly Arg Gly Val Leu Pro Ala
 65 70 75 80
 Val Glu Leu Ala Ile Glu Gln Ile Arg Asn Glu Ser Leu Leu Arg Pro
 85 90 95
 Tyr Phe Leu Asp Leu Arg Leu Tyr Asp Thr Glu Cys Asp Asn Ala Lys
 100 105 110
 Gly Leu Lys Ala Phe Tyr Asp Ala Ile Lys Tyr Gly Pro Asn His Leu
 115 120 125
 Met Val Phe Gly Gly Val Cys Pro Ser Val Thr Ser Ile Ile Ala Glu
 130 135 140
 Ser Leu Gln Gly Trp Asn Leu Val Gln Leu Ser Phe Ala Ala Thr Thr
 145 150 155 160
 Pro Val Leu Ala Asp Lys Lys Lys Tyr Pro Tyr Phe Phe Arg Thr Val
 165 170 175
 Pro Ser Asp Asn Ala Val Asn Pro Ala Ile Leu Lys Leu Leu Lys His
 180 185 190
 Tyr Gln Trp Lys Arg Val Gly Thr Leu Thr Gln Asp Val Gln Arg Phe
 195 200 205
 Ser Glu Val Arg Asn Asp Leu Thr Gly Val Leu Tyr Gly Glu Asp Ile
 210 215 220
 Glu Ile Ser Asp Thr Glu Ser Phe Ser Asn Asp Pro Cys Thr Ser Val
 225 230 235 240
 Lys Lys Leu Lys Gly Asn Asp Val Arg Ile Ile Leu Gly Gln Phe Asp
 245 250 255
 Gln Asn Met Ala Ala Lys Val Phe Cys Cys Ala Tyr Glu Glu Asn Met
 260 265 270
 Tyr Gly Ser Lys Tyr Gln Trp Ile Ile Pro Gly Trp Tyr Glu Pro Ser
 275 280 285
 Trp Trp Glu Gln Val His Thr Glu Ala Asn Ser Ser Arg Cys Leu Arg
 290 295 300
 Lys Asn Leu Leu Ala Ala Met Glu Gly Tyr Ile Gly Val Asp Phe Glu
 305 310 315 320

Pro	Leu	Ser	Ser	Lys	Gln	Ile	Lys	Thr	Ile	Ser	Gly	Lys	Thr	Pro	Gln	
				325					330					335		
Gln	Tyr	Glu	Arg	Glu	Tyr	Asn	Asn	Lys	Arg	Ser	Gly	Val	Gly	Pro	Ser	
			340					345					350			
Lys	Phe	His	Gly	Tyr	Ala	Tyr	Asp	Gly	Ile	Trp	Val	Ile	Ala	Lys	Thr	
		355					360					365				
Leu	Gln	Arg	Ala	Met	Glu	Thr	Leu	His	Ala	Ser	Ser	Arg	His	Gln	Arg	
	370					375					380					
Ile	Gln	Asp	Phe	Asn	Tyr	Thr	Asp	His	Thr	Leu	Gly	Arg	Ile	Ile	Leu	
385					390					395					400	
Asn	Ala	Met	Asn	Glu	Thr	Asn	Phe	Phe	Gly	Val	Thr	Gly	Gln	Val	Val	
				405					410					415		
Phe	Arg	Asn	Gly	Glu	Arg	Met	Gly	Thr	Ile	Lys	Phe	Thr	Gln	Phe	Gln	
			420					425					430			
Asp	Ser	Arg	Glu	Val	Lys	Val	Gly	Glu	Tyr	Asn	Ala	Val	Ala	Asp	Thr	
		435					440					445				
Leu	Glu	Ile	Ile	Asn	Asp	Thr	Ile	Arg	Phe	Gln	Gly	Ser	Glu	Pro	Pro	
	450					455					460					
Lys	Asp	Lys	Thr	Ile	Ile	Leu	Glu	Gln	Leu	Arg	Lys	Ile	Ser	Leu	Pro	
465					470					475					480	

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<212>	PRT
<213>	Human

<400> 5

Met	Val	Cys	Glu	Gly	Lys	Arg	Ser	Ala	Ser	Cys	Pro	Cys	Phe	Leu
1				5					10				15	
Leu	Thr	Ala	Lys	Phe	Tyr	Trp	Ile	Leu	Thr	Met	Met	Gln	Arg	Thr
			20					25					30	His
Ser	Gln	Glu	Tyr	Ala	His	Ser	Ile	Arg	Val	Asp	Gly	Asp	Ile	Ile
		35					40					45		Leu
Gly	Gly	Leu	Phe	Pro	Val	His	Ala	Lys	Gly	Glu	Arg	Gly	Val	Pro
	50					55					60			Cys
Gly	Glu	Leu	Lys	Lys	Glu	Lys	Gly	Ile	His	Arg	Leu	Glu	Ala	Met
65					70					75				80

10

Tyr Ala Ile Asp Gln Ile Asn Lys Asp Pro Asp Leu Leu Ser Asn Ile
 85 90 95
 Thr Leu Gly Val Arg Ile Leu Asp Thr Cys Ser Arg Asp Thr Tyr Ala
 100 105 110
 Leu Glu Gln Ser Leu Thr Phe Val Gln Ala Leu Ile Glu Lys Asp Ala
 115 120 125
 Ser Asp Val Lys Cys Ala Asn Gly Asp Pro Pro Ile Phe Thr Lys Pro
 130 135 140
 Asp Lys Ile Ser Gly Val Ile Gly Ala Ala Ala Ser Ser Val Ser Ile
 145 150 155 160
 Met Val Ala Asn Ile Leu Arg Leu Phe Lys Ile Pro Gln Ile Ser Tyr
 165 170 175
 Ala Ser Thr Ala Pro Glu Leu Ser Asp Asn Thr Arg Tyr Asp Phe Phe
 180 185 190
 Ser Arg Val Val Pro Pro Asp Ser Tyr Gln Ala Gln Ala Met Val Asp
 195 200 205
 Ile Val Thr Ala Leu Gly Trp Asn Tyr Val Ser Thr Leu Ala Ser Glu
 210 215 220
 Gly Asn Tyr Gly Glu Ser Gly Val Glu Ala Phe Thr Gln Ile Ser Arg
 225 230 235 240
 Glu Ile Gly Gly Val Cys Ile Ala Gln Ser Gln Lys Ile Pro Arg Glu
 245 250 255
 Pro Arg Pro Gly Glu Phe Glu Lys Ile Ile Lys Arg Leu Leu Glu Thr
 260 265 270
 Pro Asn Ala Arg Ala Val Ile Met Phe Ala Asn Glu Asp Asp Ile Arg
 275 280 285
 Arg Ile Leu Glu Ala Ala Lys Lys Leu Asn Gln Ser Gly His Phe Leu
 290 295 300
 Trp Ile Gly Ser Asp Ser Trp Gly Ser Lys Ile Ala Pro Val Tyr Gln
 305 310 315 320
 Gln Glu Glu Ile Ala Glu Gly Ala Val Thr Ile Leu Pro Lys Arg Ala
 325 330 335
 Ser Ile Asp Gly Phe Asp Arg Tyr Phe Arg Ser Arg Thr Leu Ala Asn
 340 345 350
 Asn Arg Arg Asn Val Trp Phe Ala Glu Phe Trp Glu Glu Asn Phe Gly
 355 360 365

11

Cys Lys Leu Gly Ser His Gly Lys Arg Asn Ser His Ile Lys Lys Cys
 370 375 380
 Thr Gly Leu Glu Arg Ile Ala Arg Asp Ser Ser Tyr Glu Gln Glu Gly
 385 390 395 400
 Lys Val Gln Phe Val Ile Asp Ala Val Tyr Ser Met Ala Tyr Ala Leu
 405 410 415
 His Asn Met His Lys Asp Leu Cys Pro Gly Tyr Ile Gly Leu Cys Pro
 420 425 430
 Arg Met Ser Thr Ile Asp Gly Lys Glu Leu Leu Gly Tyr Ile Arg Ala
 435 440 445
 Val Asn Phe Asn Gly Ser Ala Gly Thr Pro Val Thr Phe Asn Glu Asn
 450 455 460
 Gly Asp Ala Pro Gly Arg Tyr Asp Ile Phe Gln Tyr Gln Ile Thr Asn
 465 470 475 480
 Lys Ser Thr Glu Tyr Lys Val Ile Gly His Trp Thr Asn Gln Leu His
 485 490 495
 Leu Lys Val Glu Asp Met Gln Trp Ala His Arg Glu His Thr His Pro
 500 505 510
 Ala Ser Val Cys Ser Leu Pro Cys Lys Pro Gly Glu Arg Lys Lys Thr
 515 520 525
 Val Lys Gly Val Pro Cys Cys Trp His Cys Glu Arg Cys Glu Gly Tyr
 530 535 540
 Asn Tyr Gln Val Asp Glu Leu Ser Cys Glu Leu Cys Pro Leu Asp Gln
 545 550 555 560
 Arg Pro Asn Met Asn Arg Thr Gly Cys Gln Leu Ile Pro Ile Ile Lys
 565 570 575
 Leu Glu Trp His Ser Pro Trp
 580

<210> 6

<211> 250

<212> PRT

<213> Human

<400> 6

Gly Ile Ala Leu Thr Leu Phe Ala Val Leu Gly Ile Phe Leu Thr Ala
 1 5 10 15

12

Phe Val Leu Gly Val Phe Ile Lys Phe Arg Asn Thr Pro Ile Val Lys
 20 25 30
 Ala Thr Asn Arg Glu Leu Ser Tyr Leu Leu Leu Phe Ser Leu Leu Cys
 35 40 45
 Cys Phe Ser Ser Ser Leu Phe Phe Ile Gly Glu Pro Gln Asp Trp Thr
 50 55 60
 Cys Arg Leu Arg Gln Pro Ala Phe Gly Ile Ser Phe Val Leu Cys Ile
 65 70 75 80
 Ser Cys Ile Leu Val Lys Thr Asn Arg Val Leu Leu Val Phe Glu Ala
 85 90 95
 Lys Ile Pro Thr Ser Phe His Arg Lys Trp Trp Gly Leu Asn Leu Gln
 100 105 110
 Phe Leu Leu Val Phe Leu Cys Thr Phe Met Gln Ile Val Ile Cys Val
 115 120 125
 Ile Trp Leu Tyr Thr Ala Pro Pro Ser Ser Tyr Arg Asn Gln Glu Leu
 130 135 140
 Glu Asp Glu Ile Ile Phe Ile Thr Cys His Glu Gly Ser Leu Met Ala
 145 150 155 160
 Leu Gly Phe Leu Ile Gly Tyr Thr Cys Leu Leu Ala Ala Ile Cys Phe
 165 170 175
 Phe Phe Ala Phe Lys Ser Arg Lys Leu Pro Glu Asn Phe Asn Glu Ala
 180 185 190
 Lys Phe Ile Thr Phe Ser Met Leu Ile Phe Phe Ile Val Trp Ile Ser
 195 200 205
 Phe Ile Pro Ala Tyr Ala Ser Thr Tyr Gly Lys Phe Val Ser Ala Val
 210 215 220
 Glu Val Ile Ala Ile Leu Ala Ala Ser Phe Gly Leu Leu Ala Cys Ile
 225 230 235 240
 Phe Phe Asn Lys Ile Tyr Ile Ile Leu Phe
 245 250

<210> 7
 <211> 267
 <212> PRT
 <213> Human

<400> 7

Leu Phe Ile Ser Val Ser Val Leu Ser Ser Leu Gly Ile Val Leu Ala
 1 5 10 15
 Val Val Cys Leu Ser Phe Asn Ile Tyr Asn Ser His Val Arg Tyr Ile
 20 25 30
 Gln Asn Ser Gln Pro Asn Leu Asn Asn Leu Thr Ala Val Gly Cys Ser
 35 40 45
 Leu Ala Leu Ala Ala Val Phe Pro Leu Gly Leu Asp Gly Tyr His Ile
 50 55 60
 Gly Arg Asn Gln Phe Pro Phe Val Cys Gln Ala Arg Leu Trp Leu Leu
 65 70 75 80
 Gly Leu Gly Phe Ser Leu Gly Tyr Gly Ser Met Phe Thr Lys Ile Trp
 85 90 95
 Trp Val His Thr Val Phe Thr Lys Lys Glu Glu Lys Lys Glu Trp Arg
 100 105 110
 Lys Thr Leu Glu Pro Trp Lys Leu Tyr Ala Thr Val Gly Leu Leu Val
 115 120 125
 Gly Met Asp Val Leu Thr Leu Ala Ile Trp Gln Ile Val Asp Pro Leu
 130 135 140
 His Arg Thr Ile Glu Thr Phe Ala Lys Glu Glu Pro Lys Glu Asp Ile
 145 150 155 160
 Asp Val Ser Ile Leu Pro Gln Leu Glu His Cys Ser Ser Arg Lys Met
 165 170 175
 Asn Thr Trp Leu Gly Ile Phe Tyr Gly Tyr Lys Gly Leu Leu Leu Leu
 180 185 190
 Leu Gly Ile Phe Leu Ala Tyr Glu Thr Lys Ser Val Ser Thr Glu Lys
 195 200 205
 Ile Asn Asp His Arg Ala Val Gly Met Ala Ile Tyr Asn Val Ala Val
 210 215 220
 Leu Cys Leu Ile Thr Ala Pro Val Thr Met Ile Leu Ser Ser Gln Gln
 225 230 235 240
 Asp Ala Ala Phe Ala Phe Ala Ser Leu Ala Ile Val Phe Ser Ser Tyr
 245 250 255
 Ile Thr Leu Val Val Leu Phe Val Pro Lys Met
 260 265

<210> 8
 <211> 267
 <212> PRT
 <213> Human

<400> 8

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Leu Phe Ile Ser Val Ser Val Leu Ser Ser Leu Gly Ile Val Leu Ala
 1              5              10              15

Val Val Cys Leu Ser Phe Asn Ile Tyr Asn Ser His Val Arg Tyr Ile
      20              25              30

Gln Asn Ser Gln Pro Asn Leu Asn Asn Leu Thr Ala Val Gly Cys Ser
      35              40              45

Leu Ala Leu Ala Ala Val Phe Pro Leu Gly Leu Asp Gly Tyr His Ile
 50              55              60

Gly Arg Asn Gln Phe Pro Phe Val Cys Gln Ala Arg Leu Trp Leu Leu
 65              70              75              80

Gly Leu Gly Phe Ser Leu Gly Tyr Gly Ser Met Phe Thr Lys Ile Trp
      85              90              95

Trp Val His Thr Val Phe Thr Lys Lys Glu Glu Lys Lys Glu Trp Arg
      100              105              110

Lys Thr Leu Glu Pro Trp Lys Leu Tyr Ala Thr Val Gly Leu Leu Val
      115              120              125

Gly Met Asp Val Leu Thr Leu Ala Ile Trp Gln Ile Val Asp Pro Leu
      130              135              140

His Arg Thr Ile Glu Thr Phe Ala Lys Glu Glu Pro Lys Glu Asp Ile
      145              150              155              160

Asp Val Ser Ile Leu Pro Gln Leu Glu His Cys Ser Ser Arg Lys Met
      165              170              175

Asn Thr Trp Leu Gly Ile Phe Tyr Gly Tyr Lys Gly Leu Leu Leu Leu
      180              185              190

Leu Gly Ile Phe Leu Ala Tyr Glu Thr Lys Ser Val Ser Thr Glu Lys
      195              200              205

Ile Asn Asp His Arg Ala Val Gly Met Ala Ile Tyr Asn Val Ala Val
      210              215              220

Leu Cys Leu Ile Thr Ala Pro Val Thr Met Ile Leu Ser Ser Gln Gln
      225              230              235              240

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15

Asp Ala Ala Phe Ala Phe Ala Ser Leu Ala Ile Val Phe Ser Ser Tyr
 245 250 255

Ile Thr Leu Val Val Leu Phe Val Pro Lys Met
 260 265

<210> 9
 <211> 264
 <212> PRT
 <213> Human

<400> 9

Leu Tyr Ser Ile Leu Ser Ala Leu Thr Ile Leu Gly Met Ile Met Ala
 1 5 10 15

Ser Ala Phe Leu Phe Phe Asn Ile Lys Asn Arg Asn Gln Lys Leu Ile
 20 25 30

Lys Met Ser Ser Pro Tyr Met Asn Asn Leu Ile Ile Leu Gly Gly Met
 35 40 45

Leu Ser Tyr Ala Ser Ile Phe Leu Phe Gly Leu Asp Gly Ser Phe Val
 50 55 60

Ser Glu Lys Thr Phe Glu Thr Leu Cys Thr Val Arg Thr Trp Ile Leu
 65 70 75 80

Thr Val Gly Tyr Thr Thr Ala Phe Gly Ala Met Phe Ala Lys Thr Trp
 85 90 95

Arg Val His Ala Ile Phe Lys Asn Val Lys Met Lys Lys Lys Ile Ile
 100 105 110

Lys Asp Gln Lys Leu Leu Val Ile Val Gly Gly Met Leu Leu Ile Asp
 115 120 125

Leu Cys Ile Leu Ile Cys Trp Gln Ala Val Asp Pro Leu Arg Arg Thr
 130 135 140

Val Glu Lys Tyr Ser Met Glu Pro Asp Pro Ala Gly Arg Asp Ile Ser
 145 150 155 160

Ile Arg Pro Leu Leu Glu His Cys Glu Asn Thr His Met Thr Ile Trp
 165 170 175

Leu Gly Ile Val Tyr Ala Tyr Lys Gly Leu Leu Met Leu Phe Gly Cys
 180 185 190

Phe Leu Ala Trp Glu Thr Arg Asn Val Ser Ile Pro Ala Leu Asn Asp
 195 200 205

16

Ser Lys Tyr Ile Gly Met Ser Val Tyr Asn Val Gly Ile Met Cys Ile
 210 215 220

Ile Gly Ala Ala Val Ser Phe Leu Thr Arg Asp Gln Pro Asn Val Gln
 225 230 235 240

Phe Cys Ile Val Ala Leu Val Ile Ile Phe Cys Ser Thr Ile Thr Leu
 245 250 255

Cys Leu Val Phe Val Pro Lys Leu
 260

<210> 10
 <211> 260
 <212> PRT
 <213> Human

<400> 10

Ala Val Val Pro Val Phe Val Ala Ile Leu Gly Ile Ile Ala Thr Thr
 1 5 10 15

Phe Val Ile Val Thr Phe Val Arg Tyr Asn Asp Thr Pro Ile Val Arg
 20 25 30

Ala Ser Gly Arg Glu Leu Ser Tyr Val Leu Leu Thr Gly Ile Phe Leu
 35 40 45

Cys Tyr Ser Ile Thr Phe Leu Met Ile Ala Ala Pro Asp Thr Ile Ile
 50 55 60

Cys Ser Phe Arg Arg Val Phe Leu Gly Leu Gly Met Cys Phe Ser Tyr
 65 70 75 80

Ala Ala Leu Leu Thr Lys Thr Asn Arg Ile His Arg Ile Phe Glu Gln
 85 90 95

Gly Lys Lys Ser Val Thr Ala Pro Lys Phe Ile Ser Pro Ala Ser Gln
 100 105 110

Leu Val Ile Thr Phe Ser Leu Ile Ser Val Gln Leu Leu Gly Val Phe
 115 120 125

Val Trp Phe Val Val Asp Pro Pro His Ile Ile Ile Asp Tyr Gly Glu
 130 135 140

Gln Arg Thr Leu Asp Pro Glu Lys Ala Arg Gly Val Leu Lys Cys Asp
 145 150 155 160

Ile Ser Asp Leu Ser Leu Ile Cys Ser Leu Gly Tyr Ser Ile Leu Leu
 165 170 175

17

Met Val Thr Cys Thr Val Tyr Ala Ile Lys Thr Arg Gly Val Pro Glu
 180 185 190

Thr Phe Asn Glu Ala Lys Pro Ile Gly Phe Thr Met Tyr Thr Thr Cys
 195 200 205

Ile Ile Trp Leu Ala Phe Ile Pro Ile Phe Phe Gly Thr Ala Gln Ser
 210 215 220

Ala Glu Lys Met Tyr Ile Gln Thr Thr Thr Leu Thr Val Ser Met Ser
 225 230 235 240

Leu Ser Ala Ser Val Ser Leu Gly Met Leu Tyr Met Pro Lys Val Tyr
 245 250 255

Ile Ile Ile Phe
 260

<210> 11
 <211> 216
 <212> PRT
 <213> Human

<400> 11

Lys Pro Ser Arg Asn Thr Ile Glu Glu Val Arg Cys Ser Thr Ala Ala
 1 5 10 15

His Ala Phe Lys Val Ala Ala Arg Ala Thr Leu Arg Arg Ser Asn Val
 20 25 30

Ser Arg Lys Arg Ser Ser Ser Leu Gly Gly Ser Thr Gly Ser Thr Pro
 35 40 45

Ser Ser Ser Ile Ser Ser Lys Ser Asn Ser Glu Asp Pro Phe Pro Gln
 50 55 60

Pro Glu Arg Gln Lys Gln Gln Gln Pro Leu Ala Leu Thr Gln Gln Glu
 65 70 75 80

Gln Gln Gln Gln Pro Leu Thr Leu Pro Gln Gln Gln Arg Ser Gln Gln
 85 90 95

Gln Pro Arg Cys Lys Gln Lys Val Ile Phe Gly Ser Gly Thr Val Thr
 100 105 110

Phe Ser Leu Ser Phe Asp Glu Pro Gln Lys Asn Ala Met Ala His Gly
 115 120 125

Asn Ser Thr His Gln Asn Ser Leu Glu Ala Gln Lys Ser Ser Asp Thr
 130 135 140

18

Leu Thr Arg His Gln Pro Leu Leu Pro Leu Gln Cys Gly Glu Thr Asp
 145 150 155 160
 Leu Asp Leu Thr Val Gln Glu Thr Gly Leu Gln Gly Pro Val Gly Gly
 165 170 175
 Asp Gln Arg Pro Glu Val Glu Asp Pro Glu Glu Leu Ser Pro Ala Leu
 180 185 190
 Val Val Ser Ser Ser Gln Ser Phe Val Ile Ser Gly Gly Gly Ser Thr
 195 200 205
 Val Thr Glu Asn Val Val Asn Ser
 210 215

<210> 12
 <211> 104
 <212> PRT
 <213> Human

<400> 12

Arg Arg Leu Ile Thr Arg Gly Glu Trp Gln Ser Glu Ala Gln Asp Thr
 1 5 10 15
 Met Lys Thr Gly Ser Ser Thr Asn Asn Asn Glu Glu Glu Lys Ser Arg
 20 25 30
 Leu Leu Glu Lys Glu Asn Arg Glu Leu Glu Lys Ile Ile Ala Glu Lys
 35 40 45
 Glu Glu Arg Val Ser Glu Leu Arg His Gln Leu Gln Ser Arg Gln Gln
 50 55 60
 Leu Arg Ser Arg Arg His Pro Pro Thr Pro Pro Glu Pro Ser Gly Gly
 65 70 75 80
 Leu Pro Arg Gly Pro Pro Glu Pro Pro Asp Arg Leu Ser Cys Asp Gly
 85 90 95
 Ser Arg Val His Leu Leu Tyr Lys
 100

<210> 13
 <211> 104
 <212> PRT
 <213> Human

19

<400> 13

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 Glu Glu Arg Val Ser Glu Leu Arg His Gln Leu Gln Ser Arg Gln Gln
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 Leu Arg Ser Arg Arg His Pro Pro Thr Pro Pro Glu Pro Ser Gly Gly
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 Leu Pro Arg Gly Pro Pro Glu Pro Pro Asp Arg Leu Ser Cys Asp Gly
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 Ser Arg Val His Leu Leu Tyr Lys
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 <213> Human

<400> 14

Ile Thr Leu Arg Thr Asn Pro Asp Ala Ala Thr Gln Asn Arg Arg Phe
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 Ser Glu Asn His Arg Leu Arg Met Lys Ile Thr Glu Leu Asp Lys Asp
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 Leu Glu Glu Val Thr Met Gln Leu Gln Asp Thr Pro Glu Lys Thr Thr
 65 70 75 80
 Tyr Ile Lys Gln Asn His Tyr Gln Glu Leu Asn Asp Ile Leu Asn Leu
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 Gly Asn Phe Thr Glu Ser Thr Asp Gly Gly Lys Ala Ile Leu Lys Asn
 100 105 110

20

His Leu Asp Gln Asn Pro Gln Leu Gln Trp Asn Thr Thr Glu Pro Ser
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 Arg Thr Cys Lys Asp Pro Ile Glu Asp Ile Asn Ser Pro Glu His Ile
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 Gln Arg Arg Leu Ser Leu Gln Leu Pro Ile Leu His His Ala Tyr Leu
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 Pro Ser Ile Gly Gly Val Asp Ala Ser Cys Val Ser Pro Cys Val Ser
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 Pro Thr Ala Ser Pro Arg His Arg His Val Pro Pro Ser Phe Arg Val
 180 185 190
 Met Val Ser Gly Leu
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<400> 15

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 Val Thr Ala Ala Thr Met Gln Ser Lys Leu Ile Gln Lys Gly Asn Asp
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 Asn Ser Lys Ser Ser Val Glu Phe Pro Met Val Lys Ser Gly Ser Thr
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 Ser
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<400> 16

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21

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 Leu Glu Gln Lys Lys Gln Glu Arg Glu Glu Leu Lys Leu Leu Leu Leu
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 Gly Pro Gly Glu Ser Gly Lys Ser Thr Phe Ile Lys Gln Met Arg Ile
 50 55 60
 Ile His Gly Val Gly Tyr Ser Glu Glu Asp Arg Arg Ala Phe Arg Leu
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 Leu Ile Tyr Gln Asn Ile Phe Val Ser Met Gln Ala Met Ile Asp Ala
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 Met Asp Arg Leu Gln Ile Pro Phe Ser Arg Pro Asp Ser Lys Gln His
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 Ala Ser Leu Val Met Thr Gln Asp Pro Tyr Lys Val Ser Thr Phe Glu
 115 120 125
 Lys Pro Tyr Ala Val Ala Met Gln Tyr Leu Trp Arg Asp Ala Gly Ile
 130 135 140
 Arg Ala Cys Tyr Glu Arg Arg Arg Glu Phe His Leu Leu Asp Ser Ala
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 Val Tyr Tyr Leu Ser His Leu Glu Arg Ile Ser Glu Asp Ser Tyr Ile
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 Pro Thr Ala Gln Asp Val Leu Arg Ser Arg Met Pro Thr Thr Gly Ile
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 Asn Glu Tyr Cys Phe Ser Val Lys Lys Thr Lys Leu Arg Ile Val Asp
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 Val Gly Gly Gln Arg Ser Glu Arg Arg Lys Trp Ile His Cys Phe Glu
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 Asn Val Ile Ala Leu Ile Tyr Leu Ala Ser Leu Ser Glu Tyr Asp Gln
 225 230 235 240
 Cys Leu Glu Glu Asn Asp Gln Glu Asn Arg Met Glu Glu Ser Leu Ala
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 Leu Phe Ser Thr Ile Leu Glu Leu Pro Trp Phe Lys Ser Thr Ser Val
 260 265 270
 Ile Leu Phe Leu Asn Lys Thr Asp Ile Leu Glu Asp Lys Ile His Thr
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 Ser His Leu Ala Thr Tyr Phe Pro Ser Phe Gln Gly Pro Arg Arg Asp
 290 295 300

22

Ala Glu Ala Ala Lys Ser Phe Ile Leu Asp Met Tyr Ala Arg Val Tyr
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Ala Ser Cys Ala Glu Pro Gln Asp Gly Gly Arg Lys Gly Ser Arg Ala
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Arg Arg Phe Phe Ala His Phe Thr Cys Ala Thr Asp Thr Gln Ser Val
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Arg Ser Val Phe Lys Asp Val Arg Asp Ser Val Leu Ala Arg Tyr Leu
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Asp Glu Ile Asn Leu Leu
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<400> 17

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Asp Glu Lys Ala Ala Ala Arg Val Asp Gln Glu Ile Asn Arg Ile Leu
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Gly Pro Gly Glu Ser Gly Lys Ser Thr Phe Ile Lys Gln Met Arg Ile
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Ile His Gly Ala Gly Tyr Ser Glu Glu Glu Arg Lys Gly Phe Arg Pro
 65 70 75 80

Leu Val Tyr Gln Asn Ile Phe Val Ser Met Arg Ala Met Ile Glu Ala
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Met Glu Arg Leu Gln Ile Pro Phe Ser Arg Pro Glu Ser Lys His His
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Ala Ser Leu Val Met Ser Gln Asp Pro Tyr Lys Val Thr Thr Phe Glu
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Lys Arg Tyr Ala Ala Ala Met Gln Trp Leu Trp Arg Asp Ala Gly Ile
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Arg Ala Cys Tyr Glu Arg Arg Arg Glu Phe His Leu Leu Asp Ser Ala
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23

Val Tyr Tyr Leu Ser His Leu Glu Arg Ile Thr Glu Glu Gly Tyr Val
 165 170 175

Pro Thr Ala Gln Asp Val Leu Arg Ser Arg Met Pro Thr Thr Gly Ile
 180 185 190

Asn Glu Tyr Cys Phe Ser Val Gln Lys Thr Asn Leu Arg Ile Val Asp
 195 200 205

Val Gly Gly Gln Lys Ser Glu Arg Lys Lys Trp Ile His Cys Phe Glu
 210 215 220

Asn Val Ile Ala Leu Ile Tyr Leu Ala Ser Leu Ser Glu Tyr Asp Gln
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Cys Leu Glu Glu Asn Asn Gln Glu Asn Arg Met Lys Glu Ser Leu Ala
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Leu Phe Gly Thr Ile Leu Glu Leu Pro Trp Phe Lys Ser Thr Ser Val
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Ile Leu Phe Leu Asn Lys Thr Asp Ile Leu Glu Glu Lys Ile Pro Thr
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Ser His Leu Ala Thr Tyr Phe Pro Ser Phe Gln Gly Pro Lys Gln Asp
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Ala Glu Ala Ala Lys Arg Phe Ile Leu Asp Met Tyr Thr Arg Met Tyr
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Thr Gly Cys Val Asp Gly Pro Glu Gly Ser Lys Lys Gly Ala Arg Ser
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Arg Arg Leu Phe Ser His Tyr Thr Cys Ala Thr Asp Thr Gln Asn Ile
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<212> DNA

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<400> 19

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<212> DNA

<213> Rat

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Gln Val Lys Ala Ile Asn Phe Leu Pro Val Asp Tyr Glu Ile Glu Tyr
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33

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 Glu Arg Arg Ala Val Tyr Ile Gly Ala Leu Phe Pro Met Ser Gly Gly
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 Trp Pro Gly Gly Gln Ala Cys Gln Pro Ala Val Glu Met Ala Leu Glu
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 Asp Val Asn Ser Arg Arg Asp Ile Leu Pro Asp Tyr Glu Leu Lys Leu
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 Ile His His Asp Ser Lys Cys Asp Pro Gly Gln Ala Thr Lys Tyr Leu
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 Tyr Glu Leu Leu Tyr Asn Asp Pro Ile Lys Ile Ile Leu Met Pro Gly
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 Cys Ser Ser Val Ser Thr Leu Val Ala Glu Ala Ala Arg Met Trp Asn
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 Val Phe Cys Glu Val Tyr Lys Glu Arg Leu Phe Gly Lys Lys Tyr Val
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Trp Phe Leu Ile Gly Trp Tyr Ala Asp Asn Trp Phe Lys Thr Tyr Asp
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 Glu Lys Ser Arg Leu Leu Glu Lys Glu Asn Arg Glu Leu Glu Lys Ile
 770 775 780
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 Ser Arg Gln Gln Leu Arg Ser Arg Arg His Pro Pro Thr Pro Pro Asp
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 <213> Human

<400> 26

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Val Leu Gly Gly Leu Phe Pro Val His Gln Lys Gly Gly Pro Ala Glu
      35              40              45

Asp Cys Gly Pro Val Asn Glu His Arg Gly Ile Gln Arg Leu Glu Ala
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Met Leu Phe Ala Leu Asp Arg Ile Asn Arg Asp Pro His Leu Leu Pro
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Gly Val Arg Leu Gly Ala His Ile Leu Asp Ser Cys Ser Lys Asp Thr
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His Ala Leu Glu Gln Ala Leu Asp Phe Val Arg Ala Ser Leu Ser Arg
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Gly Ala Asp Gly Ser Arg His Ile Cys Pro Asp Gly Ser Tyr Ala Thr
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His Gly Asp Ala Pro Thr Ala Ile Thr Gly Val Ile Gly Gly Ser Tyr
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Ser Asp Val Ser Ile Gln Val Ala Asn Leu Leu Arg Leu Phe Gln Ile
145              150              155              160

Pro Gln Ile Ser Tyr Ala Ser Thr Ser Ala Lys Leu Ser Asp Lys Ser
      165              170              175

Arg Tyr Asp Tyr Phe Ala Arg Thr Val Pro Pro Asp Phe Phe Gln Ala
      180              185              190

Lys Ala Met Ala Glu Ile Leu Arg Phe Phe Asn Trp Thr Tyr Val Ser
      195              200              205

Thr Glu Ala Ser Glu Gly Asp Tyr Gly Glu Thr Gly Ile Glu Ala Phe
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Val Gly Arg Ala Met Ser Arg Ala Ala Phe Glu Gly Val Val Arg Ala
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39

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 Ser Tyr Pro Ile Ser Asp Phe Ala Ser Tyr Phe Gln Ser Leu Asp Pro
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 Ile Arg Trp Gly Asp Ala Trp Ala Val Gly Pro Val Thr Ile Ala Cys
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 Asn Ala Thr Pro Val Val Lys Ala Ser Gly Arg Glu Leu Cys Tyr Ile
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 Ala Lys Pro Ser Thr Ala Val Cys Thr Leu Arg Arg Leu Gly Leu Gly
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 Ile Ala Arg Ile Phe Gly Gly Ala Arg Glu Gly Ala Gln Arg Pro Arg
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 Thr Gly Lys Glu Thr Ala Pro Glu Arg Arg Glu Val Val Thr Leu Arg
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 Cys Asn His Arg Asp Ala Ser Met Leu Gly Ser Leu Ala Tyr Asn Val
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 Leu Leu Ile Ala Leu Cys Thr Leu Tyr Ala Phe Asn Thr Arg Lys Cys
 740 745 750
 Pro Glu Asn Phe Asn Glu Ala Lys Phe Ile Gly Phe Thr Met Tyr Thr
 755 760 765
 Thr Cys Ile Ile Trp Leu Ala Leu Leu Pro Ile Phe Tyr Val Thr Ser
 770 775 780
 Ser Asp Tyr Arg Val Gln Thr Thr Thr Met Cys Val Ser Val Ser Leu
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 <211> 1077
 <212> DNA
 <213> Artificial Sequence

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 <223> Chimeric Gqi5

<400> 28

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Lys Arg Asp Ala Arg Arg Glu Leu Lys Leu Leu Leu Gly Thr Gly
35            40            45

Glu Ser Gly Lys Ser Thr Phe Ile Lys Gln Met Arg Ile Ile His Gly
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Ser Gly Tyr Ser Asp Glu Asp Lys Arg Gly Phe Thr Lys Leu Val Tyr
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42

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 Glu Ser Asp Asn Glu Asn Arg Met Glu Glu Ser Lys Ala Leu Phe Arg
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 <213> Artificial Sequence

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<213> Artificial Sequence

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<220>
<223> Chimeric hCAR/hmGluR2

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<400> 31

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Ile Leu Gly Gly Leu Phe Pro Ile His Phe Gly Val Ala Ala Lys Asp
      35             40             45

Gln Asp Leu Lys Ser Arg Pro Glu Ser Val Glu Cys Ile Arg Tyr Asn
      50             55             60

Phe Arg Gly Phe Arg Trp Leu Gln Ala Met Ile Phe Ala Ile Glu Glu
      65             70             75             80

Ile Asn Ser Ser Pro Ala Leu Leu Pro Asn Leu Thr Leu Gly Tyr Arg
      85             90             95

Ile Phe Asp Thr Cys Asn Thr Val Ser Lys Ala Leu Glu Ala Thr Leu
      100            105            110

Ser Phe Val Ala Gln Asn Lys Ile Asp Ser Leu Asn Leu Asp Glu Phe
      115            120            125

Cys Asn Cys Ser Glu His Ile Pro Ser Thr Ile Ala Val Val Gly Ala
      130            135            140

Thr Gly Ser Gly Val Ser Thr Ala Val Ala Asn Leu Leu Gly Leu Phe
      145            150            155            160

Tyr Ile Pro Gln Val Ser Tyr Ala Ser Ser Ser Arg Leu Leu Ser Asn
      165            170            175

Lys Asn Gln Phe Lys Ser Phe Leu Arg Thr Ile Pro Asn Asp Glu His
      180            185            190

Gln Ala Thr Ala Met Ala Asp Ile Ile Glu Tyr Phe Arg Trp Asn Trp
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45

Val Gly Thr Ile Ala Ala Asp Asp Asp Tyr Gly Arg Pro Gly Ile Glu
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 Lys Phe Arg Glu Glu Ala Glu Glu Arg Asp Ile Cys Ile Asp Phe Ser
 225 230 235 240
 Glu Leu Ile Ser Gln Tyr Ser Asp Glu Glu Glu Ile Gln His Val Val
 245 250 255
 Glu Val Ile Gln Asn Ser Thr Ala Lys Val Ile Val Val Phe Ser Ser
 260 265 270
 Gly Pro Asp Leu Glu Pro Leu Ile Lys Glu Ile Val Arg Arg Asn Ile
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 Thr Gly Lys Ile Trp Leu Ala Ser Glu Ala Trp Ala Ser Ser Ser Leu
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 Ile Ala Met Pro Gln Tyr Phe His Val Val Gly Gly Thr Ile Gly Phe
 305 310 315 320
 Ala Leu Lys Ala Gly Gln Ile Pro Gly Phe Arg Glu Phe Leu Lys Lys
 325 330 335
 Val His Pro Arg Lys Ser Val His Asn Gly Phe Ala Lys Glu Phe Trp
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 Glu Glu Thr Phe Asn Cys His Leu Gln Glu Gly Ala Lys Gly Pro Leu
 355 360 365
 Pro Val Asp Thr Phe Leu Arg Gly His Glu Glu Ser Gly Asp Arg Phe
 370 375 380
 Ser Asp Ser Ser Thr Ala Phe Arg Pro Leu Cys Thr Gly Asp Glu Asn
 385 390 395 400
 Ile Ser Ser Val Glu Thr Pro Tyr Ile Asp Tyr Thr His Leu Arg Ile
 405 410 415
 Ser Tyr Asn Val Tyr Leu Ala Val Tyr Ser Ile Ala His Ala Leu Gln
 420 425 430
 Asp Ile Tyr Thr Cys Leu Pro Gly Arg Gly Leu Phe Thr Asn Gly Ser
 435 440 445
 Cys Ala Asp Ile Lys Lys Val Glu Ala Trp Gln Val Leu Lys His Leu
 450 455 460
 Arg His Leu Asn Phe Thr Asn Asn Met Gly Glu Gln Val Thr Phe Asp
 465 470 475 480
 Glu Cys Gly Asp Leu Val Gly Asn Tyr Ser Ile Ile Asn Trp His Leu
 485 490 495

Ser Pro Glu Asp Gly Ser Ile Val Phe Lys Glu Val Gly Tyr Tyr Asn
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 Val Tyr Ala Lys Lys Gly Glu Arg Leu Phe Ile Asn Glu Glu Lys Ile
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 Leu Trp Ser Gly Phe Ser Arg Glu Val Pro Phe Ser Asn Cys Ser Arg
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 Asp Cys Leu Ala Gly Thr Arg Lys Gly Ile Ile Glu Gly Glu Pro Thr
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 Cys Cys Phe Glu Cys Val Glu Cys Pro Asp Gly Glu Tyr Ser Asp Glu
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 Thr Asp Ala Ser Ala Cys Asn Lys Cys Pro Asp Asp Phe Trp Ser Asn
 580 585 590
 Glu Asn His Thr Ser Cys Phe Glu Leu Pro Gln Glu Tyr Ile Arg Trp
 595 600 605
 Gly Asp Ala Trp Ala Val Gly Pro Val Thr Ile Ala Cys Leu Gly Ala
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 Leu Ala Thr Leu Phe Val Leu Gly Val Phe Val Arg His Asn Ala Thr
 625 630 635 640
 Pro Val Val Lys Ala Ser Gly Arg Glu Leu Cys Tyr Ile Leu Leu Gly
 645 650 655
 Gly Val Phe Leu Cys Tyr Cys Met Thr Phe Ile Phe Ile Ala Lys Pro
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 Ser Thr Ala Val Cys Thr Leu Arg Arg Leu Gly Leu Gly Thr Ala Phe
 675 680 685
 Ser Val Cys Tyr Ser Ala Leu Leu Thr Lys Thr Asn Arg Ile Ala Arg
 690 695 700
 Ile Phe Gly Gly Ala Arg Glu Gly Ala Gln Arg Pro Arg Phe Ile Ser
 705 710 715 720
 Pro Ala Ser Gln Val Ala Ile Cys Leu Ala Leu Ile Ser Gly Gln Leu
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 Leu Ile Val Val Ala Trp Leu Val Val Glu Ala Pro Gly Thr Gly Lys
 740 745 750
 Glu Thr Ala Pro Glu Arg Arg Glu Val Val Thr Leu Arg Cys Asn His
 755 760 765
 Arg Asp Ala Ser Met Leu Gly Ser Leu Ala Tyr Asn Val Leu Leu Ile
 770 775 780

47

Ala Leu Cys Thr Leu Tyr Ala Phe Asn Thr Arg Lys Cys Pro Glu Asn
785 790 795 800

Phe Asn Glu Ala Lys Phe Ile Gly Phe Thr Met Tyr Thr Thr Cys Ile
805 810 815

Ile Trp Leu Ala Leu Leu Pro Ile Phe Tyr Val Thr Ser Ser Asp Tyr
820 825 830

Arg Val Gln Thr Thr Thr Met Cys Val Ser Val Ser Leu Ser Gly Ser
835 840 845

Val Val Leu Gly Cys Leu Phe Ala Pro Lys Leu His Ile Ile Leu Phe
850 855 860

Gln Pro Gln Lys Asn Val Val Ser His Arg Ala Pro Thr Ser Arg Phe
865 870 875 880

Gly Ser Ala Ala Ala Arg Ala Ser Ser Ser Leu Gly Gln Gly Ser Gly
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Ser Gln Phe Val Pro Thr Val Cys Asn Gly Arg Glu Val Val Asp Ser
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Thr Thr Ser Ser Leu
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<211> 3831

<212> DNA

<213> Artificial Sequence

<220>

<223> Chimeric phCaR/hmGluR2*Gqi5

<400> 32

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<210> 33
 <211> 1276
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 <213> Artificial Sequence

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 <223> Chimeric phCaR/hmGluR2*Gqi5

<400> 33

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Thr	Ser	Ala	Tyr	Gly	Pro	Asp	Gln	Arg	Ala	Gln	Lys	Lys	Gly	Asp	Ile	20	25	30	
Ile	Leu	Gly	Gly	Leu	Phe	Pro	Ile	His	Phe	Gly	Val	Ala	Ala	Lys	Asp	35	40	45	
Gln	Asp	Leu	Lys	Ser	Arg	Pro	Glu	Ser	Val	Glu	Cys	Ile	Arg	Tyr	Asn	50	55	60	
Phe	Arg	Gly	Phe	Arg	Trp	Leu	Gln	Ala	Met	Ile	Phe	Ala	Ile	Glu	Glu	65	70	75	80
Ile	Asn	Ser	Ser	Pro	Ala	Leu	Leu	Pro	Asn	Leu	Thr	Leu	Gly	Tyr	Arg	85	90	95	
Ile	Phe	Asp	Thr	Cys	Asn	Thr	Val	Ser	Lys	Ala	Leu	Glu	Ala	Thr	Leu	100	105	110	
Ser	Phe	Val	Ala	Gln	Asn	Lys	Ile	Asp	Ser	Leu	Asn	Leu	Asp	Glu	Phe	115	120	125	
Cys	Asn	Cys	Ser	Glu	His	Ile	Pro	Ser	Thr	Ile	Ala	Val	Val	Gly	Ala	130	135	140	
Thr	Gly	Ser	Gly	Val	Ser	Thr	Ala	Val	Ala	Asn	Leu	Leu	Gly	Leu	Phe	145	150	155	160
Tyr	Ile	Pro	Gln	Val	Ser	Tyr	Ala	Ser	Ser	Ser	Arg	Leu	Leu	Ser	Asn	165	170	175	
Lys	Asn	Gln	Phe	Lys	Ser	Phe	Leu	Arg	Thr	Ile	Pro	Asn	Asp	Glu	His	180	185	190	
Gln	Ala	Thr	Ala	Met	Ala	Asp	Ile	Ile	Glu	Tyr	Phe	Arg	Trp	Asn	Trp	195	200	205	
Val	Gly	Thr	Ile	Ala	Ala	Asp	Asp	Asp	Tyr	Gly	Arg	Pro	Gly	Ile	Glu	210	215	220	
Lys	Phe	Arg	Glu	Glu	Ala	Glu	Glu	Arg	Asp	Ile	Cys	Ile	Asp	Phe	Ser	225	230	235	240

50

Glu Leu Ile Ser Gln Tyr Ser Asp Glu Glu Glu Ile Gln His Val Val
 245 250 255
 Glu Val Ile Gln Asn Ser Thr Ala Lys Val Ile Val Val Phe Ser Ser
 260 265 270
 Gly Pro Asp Leu Glu Pro Leu Ile Lys Glu Ile Val Arg Arg Asn Ile
 275 280 285
 Thr Gly Lys Ile Trp Leu Ala Ser Glu Ala Trp Ala Ser Ser Ser Leu
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 Ile Ala Met Pro Gln Tyr Phe His Val Val Gly Gly Thr Ile Gly Phe
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 Ala Leu Lys Ala Gly Gln Ile Pro Gly Phe Arg Glu Phe Leu Lys Lys
 325 330 335
 Val His Pro Arg Lys Ser Val His Asn Gly Phe Ala Lys Glu Phe Trp
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 Glu Glu Thr Phe Asn Cys His Leu Gln Glu Gly Ala Lys Gly Pro Leu
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 Pro Val Asp Thr Phe Leu Arg Gly His Glu Glu Ser Gly Asp Arg Phe
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 Ser Asn Ser Ser Thr Ala Phe Arg Pro Leu Cys Thr Gly Asp Glu Asn
 385 390 395 400
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 405 410 415
 Ser Tyr Asn Val Tyr Leu Ala Val Tyr Ser Ile Ala His Ala Leu Gln
 420 425 430
 Asp Ile Tyr Thr Cys Leu Pro Gly Arg Gly Leu Phe Thr Asn Gly Ser
 435 440 445
 Cys Ala Asp Ile Lys Lys Val Glu Ala Trp Gln Val Leu Lys His Leu
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 465 470 475 480
 Glu Cys Gly Asp Leu Val Gly Asn Tyr Ser Ile Ile Asn Trp His Leu
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 Ser Pro Glu Asp Gly Ser Ile Val Phe Lys Glu Val Gly Tyr Tyr Asn
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 Val Tyr Ala Lys Lys Gly Glu Arg Leu Phe Ile Asn Glu Glu Lys Ile
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51

Leu Trp Ser Gly Phe Ser Arg Glu Val Pro Phe Ser Asn Cys Ser Arg
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 Asp Cys Leu Ala Gly Thr Arg Lys Gly Ile Ile Glu Gly Glu Pro Thr
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 Cys Cys Phe Glu Cys Val Glu Cys Pro Asp Gly Glu Tyr Ser Asp Glu
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 Thr Asp Ala Ser Ala Cys Asn Lys Cys Pro Asp Asp Phe Trp Ser Asn
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 595 600 605
 Gly Asp Ala Trp Ala Val Gly Pro Val Thr Ile Ala Cys Leu Gly Ala
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 Pro Val Val Lys Ala Ser Gly Arg Glu Leu Cys Tyr Ile Leu Leu Gly
 645 650 655
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 Glu Thr Ala Pro Glu Arg Arg Glu Val Val Thr Leu Arg Cys Asn His
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 Ala Leu Cys Thr Leu Tyr Ala Phe Asn Thr Arg Lys Cys Pro Glu Asn
 785 790 795 800
 Phe Asn Glu Ala Lys Phe Ile Gly Phe Thr Met Tyr Thr Thr Cys Ile
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 Ser Thr Lys Tyr Tyr Leu Asn Asp Leu Asp Arg Val Ala Asp Pro Ala
 1075 1080 1085
 Tyr Leu Pro Thr Gln Gln Asp Val Leu Arg Val Arg Val Pro Thr Thr
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53

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 Val Asp Val Gly Gly Gln Arg Ser Glu Arg Arg Lys Trp Ile His Cys
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 Lys Ala Leu Phe Arg Thr Ile Ile Thr Tyr Pro Trp Phe Gln Asn Ser
 1170 1175 1180
 Ser Val Ile Leu Phe Leu Asn Lys Lys Asp Leu Leu Glu Glu Lys Ile
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 <223> Chimeric hmGluR2/hCaR

<400> 34

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<210> 35

<211> 1035

<212> PRT

<213> Artificial Sequence

<220>

<223> Chimeric hmGluR2/hCaR

55

<400> 35

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 35 40 45
 Asp Cys Gly Pro Val Asn Glu His Arg Gly Ile Gln Arg Leu Glu Ala
 50 55 60
 Met Leu Phe Ala Leu Asp Arg Ile Asn Arg Asp Pro His Leu Leu Pro
 65 70 75 80
 Gly Val Arg Leu Gly Ala His Ile Leu Asp Ser Cys Ser Lys Asp Thr
 85 90 95
 His Ala Leu Glu Gln Ala Leu Asp Phe Val Arg Ala Ser Leu Ser Arg
 100 105 110
 Gly Ala Asp Gly Ser Arg His Ile Cys Pro Asp Gly Ser Tyr Ala Thr
 115 120 125
 His Gly Asp Ala Pro Thr Ala Ile Thr Gly Val Ile Gly Gly Ser Tyr
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 Ser Asp Val Ser Ile Gln Val Ala Asn Leu Leu Arg Leu Phe Gln Ile
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 Pro Gln Ile Ser Tyr Ala Ser Thr Ser Ala Lys Leu Ser Asp Lys Ser
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 Arg Tyr Asp Tyr Phe Ala Arg Thr Val Pro Pro Asp Phe Phe Gln Ala
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 Lys Ala Met Ala Glu Ile Leu Arg Phe Phe Asn Trp Thr Tyr Val Ser
 195 200 205
 Thr Val Ala Ser Glu Gly Asp Tyr Gly Glu Thr Gly Ile Glu Ala Phe
 210 215 220
 Glu Leu Glu Ala Arg Ala Arg Asn Ile Cys Val Ala Thr Ser Glu Lys
 225 230 235 240
 Val Gly Arg Ala Met Ser Arg Ala Ala Phe Glu Gly Val Val Arg Ala
 245 250 255
 Leu Leu Gln Lys Pro Ser Ala Arg Val Ala Val Leu Phe Thr Arg Ser
 260 265 270

56

Glu Asp Ala Arg Glu Leu Leu Ala Ala Ser Gln Arg Leu Asn Ala Ser
 275 280 285
 Phe Thr Trp Val Ala Ser Asp Gly Trp Gly Ala Leu Glu Ser Val Val
 290 295 300
 Ala Gly Ser Glu Gly Ala Ala Glu Gly Ala Ile Thr Ile Glu Leu Ala
 305 310 315 320
 Ser Tyr Pro Ile Ser Asp Phe Ala Ser Tyr Phe Gln Ser Leu Asp Pro
 325 330 335
 Trp Asn Asn Ser Arg Asn Pro Trp Phe Arg Glu Phe Trp Glu Gln Arg
 340 345 350
 Phe Arg Cys Ser Phe Arg Gln Arg Asp Cys Ala Ala His Ser Leu Arg
 355 360 365
 Ala Val Pro Phe Glu Gln Glu Ser Lys Ile Met Phe Val Val Asn Ala
 370 375 380
 Val Tyr Ala Met Ala His Ala Leu His Asn Met His Arg Ala Leu Cys
 385 390 395 400
 Pro Asn Thr Thr Arg Leu Cys Asp Ala Met Arg Pro Val Asn Gly Arg
 405 410 415
 Arg Leu Tyr Lys Asp Phe Val Leu Asn Val Lys Phe Asp Ala Pro Phe
 420 425 430
 Arg Pro Ala Asp Thr His Asn Glu Val Arg Phe Asp Arg Phe Gly Asp
 435 440 445
 Gly Ile Gly Arg Tyr Asn Ile Phe Thr Tyr Leu Arg Ala Gly Ser Gly
 450 455 460
 Arg Tyr Arg Tyr Gln Lys Val Gly Tyr Trp Ala Glu Gly Leu Thr Leu
 465 470 475 480
 Asp Thr Ser Leu Ile Pro Trp Ala Ser Pro Ser Ala Gly Pro Leu Pro
 485 490 495
 Ala Ser Arg Cys Ser Glu Pro Cys Leu Gln Asn Glu Val Lys Ser Val
 500 505 510
 Gln Pro Gly Glu Val Cys Cys Trp Leu Cys Ile Pro Cys Gln Pro Tyr
 515 520 525
 Glu Tyr Arg Leu Asp Glu Phe Thr Cys Ala Asp Cys Gly Leu Gly Tyr
 530 535 540
 Trp Pro Asn Ala Ser Leu Thr Gly Cys Phe Glu Leu Pro Gln Glu Tyr
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57

Ile Arg Trp Gly Asp Ala Trp Ala Val Gly Pro Val Thr Ile Ala Cys
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 Leu Gly Ala Leu Ala Thr Leu Phe Val Leu Gly Val Phe Val Arg His
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 Asn Ala Thr Pro Val Val Lys Ala Ser Gly Arg Glu Leu Cys Tyr Ile
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 Ala Lys Pro Ser Thr Ala Val Cys Thr Leu Arg Arg Leu Gly Leu Gly
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 645 650 655
 Ile Ala Arg Ile Phe Gly Gly Ala Arg Glu Gly Ala Gln Arg Pro Arg
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 Gly Gln Leu Leu Ile Val Val Ala Trp Leu Val Val Glu Ala Pro Gly
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 Thr Gly Lys Glu Thr Ala Pro Glu Arg Arg Glu Val Val Thr Leu Arg
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 Cys Asn His Arg Asp Ala Ser Met Leu Gly Ser Leu Ala Tyr Asn Val
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 Pro Glu Asn Phe Asn Glu Ala Lys Phe Ile Gly Phe Thr Met Tyr Thr
 755 760 765
 Thr Cys Ile Ile Trp Leu Ala Phe Leu Pro Ile Phe Tyr Val Thr Ser
 770 775 780
 Ser Asp Tyr Arg Val Gln Thr Thr Thr Met Cys Val Ser Val Ser Leu
 785 790 795 800
 Ser Gly Ser Val Val Leu Gly Cys Leu Phe Ala Pro Lys Leu His Ile
 805 810 815
 Ile Leu Phe Gln Pro Gln Lys Asn Thr Ile Glu Glu Val Arg Cys Ser
 820 825 830
 Thr Ala Ala His Ala Phe Lys Val Ala Ala Arg Ala Thr Leu Arg Arg
 835 840 845

58

Ser Asn Val Ser Arg Lys Arg Ser Ser Ser Leu Gly Gly Ser Thr Gly
 850 855 860
 Ser Thr Pro Ser Ser Ser Ile Ser Ser Lys Ser Asn Ser Glu Asp Pro
 865 870 875 880
 Phe Pro Gln Pro Glu Arg Gln Lys Gln Gln Gln Pro Leu Ala Leu Thr
 885 890 895
 Gln Gln Glu Gln Gln Gln Gln Pro Leu Thr Leu Pro Gln Gln Gln Arg
 900 905 910
 Ser Gln Gln Gln Pro Arg Cys Lys Gln Lys Val Ile Phe Gly Ser Gly
 915 920 925
 Thr Val Thr Phe Ser Leu Ser Phe Asp Glu Pro Gln Lys Asn Ala Met
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 Ala His Gly Asn Ser Thr His Gln Asn Ser Leu Glu Ala Gln Lys Ser
 945 950 955 960
 Ser Asp Thr Leu Thr Arg His Gln Pro Leu Leu Pro Leu Gln Cys Gly
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 Glu Thr Asp Leu Asp Leu Thr Val Gln Glu Thr Gly Leu Gln Gly Pro
 980 985 990
 Val Gly Gly Asp Gln Arg Pro Glu Val Glu Asp Pro Glu Glu Leu Ser
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<210> 36

<211> 4185

<212> DNA

<213> Artificial Sequence

<220>

<223> Chimeric pmGluR2//CaR*Gα_i5

<400> 36

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<210> 37

<211> 1394

<212> PRT

<213> Artificial Sequence

<220>

<223> Chimeric pmGluR2//CaR*G α _{i5}

<400> 37

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Val Leu Gly Gly Leu Phe Pro Val His Gln Lys Gly Gly Pro Ala Glu
35              40              45

Asp Cys Gly Pro Val Asn Glu His Arg Gly Ile Gln Arg Leu Glu Ala
50              55              60

Met Leu Phe Ala Leu Asp Arg Ile Asn Arg Asp Pro His Leu Leu Pro
65              70              75              80

Gly Val Arg Leu Gly Ala His Ile Leu Asp Ser Cys Ser Lys Asp Thr
85              90              95

His Ala Leu Glu Gln Ala Leu Asp Phe Val Arg Ala Ser Leu Ser Arg
100             105             110

Gly Ala Asp Gly Ser Arg His Ile Cys Pro Asp Gly Ser Tyr Ala Thr
115             120             125

His Gly Asp Ala Pro Thr Ala Ile Thr Gly Val Ile Gly Gly Ser Tyr
130             135             140

Ser Asp Val Ser Ile Gln Val Ala Asn Leu Leu Arg Leu Phe Gln Ile
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61

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 Lys Ala Met Ala Glu Ile Leu Arg Phe Phe Asn Trp Thr Tyr Val Ser
 195 200 205
 Thr Val Ala Ser Glu Gly Asp Tyr Gly Glu Thr Gly Ile Glu Ala Phe
 210 215 220
 Glu Leu Glu Ala Arg Ala Arg Asn Ile Cys Val Ala Thr Ser Glu Lys
 225 230 235 240
 Val Gly Arg Ala Met Ser Arg Ala Ala Phe Glu Gly Val Val Arg Ala
 245 250 255
 Leu Leu Gln Lys Pro Ser Ala Arg Val Ala Val Leu Phe Thr Arg Ser
 260 265 270
 Glu Asp Ala Arg Glu Leu Leu Ala Ala Ser Gln Arg Leu Asn Ala Ser
 275 280 285
 Phe Thr Trp Val Ala Ser Asp Gly Trp Gly Ala Leu Glu Ser Val Val
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 Ala Gly Ser Glu Gly Ala Ala Glu Gly Ala Ile Thr Ile Glu Leu Ala
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 Ser Tyr Pro Ile Ser Asp Phe Ala Ser Tyr Phe Gln Ser Leu Asp Pro
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 Trp Asn Asn Ser Arg Asn Pro Trp Phe Arg Glu Phe Trp Glu Gln Arg
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 Phe Arg Cys Ser Phe Arg Gln Arg Asp Cys Ala Ala His Ser Leu Arg
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 370 375 380
 Val Tyr Ala Met Ala His Ala Leu His Asn Met His Arg Ala Leu Cys
 385 390 395 400
 Pro Asn Thr Thr Arg Leu Cys Asp Ala Met Arg Pro Val Asn Gly Arg
 405 410 415
 Arg Leu Tyr Lys Asp Phe Val Leu Asn Val Lys Phe Asp Ala Pro Phe
 420 425 430
 Arg Pro Ala Asp Thr His Asn Glu Val Arg Phe Asp Arg Phe Gly Asp
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62

Gly Ile Gly Arg Tyr Asn Ile Phe Thr Tyr Leu Arg Ala Gly Ser Gly
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Arg Tyr Arg Tyr Gln Lys Val Gly Tyr Trp Ala Glu Gly Leu Thr Leu
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Asp Thr Ser Leu Ile Pro Trp Ala Ser Pro Ser Ala Gly Pro Leu Pro
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Ala Ser Arg Cys Ser Glu Pro Cys Leu Gln Asn Glu Val Lys Ser Val
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Gln Pro Gly Glu Val Cys Cys Trp Leu Cys Ile Pro Cys Gln Pro Tyr
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Glu Tyr Arg Leu Asp Glu Phe Thr Cys Ala Asp Cys Gly Leu Gly Tyr
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Trp Pro Asn Ala Ser Leu Thr Gly Cys Phe Glu Leu Pro Gln Glu Tyr
 545 550 555 560

Ile Arg Trp Gly Asp Ala Trp Ala Val Gly Pro Val Thr Ile Ala Cys
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Leu Gly Ala Leu Ala Thr Leu Phe Val Leu Gly Val Phe Val Arg His
 580 585 590

Asn Ala Thr Pro Val Val Lys Ala Ser Gly Arg Glu Leu Cys Tyr Ile
 595 600 605

Leu Leu Gly Gly Val Phe Leu Cys Tyr Cys Met Thr Phe Ile Phe Ile
 610 615 620

Ala Lys Pro Ser Thr Ala Val Cys Thr Leu Arg Arg Leu Gly Leu Gly
 625 630 635 640

Thr Ala Phe Ser Val Cys Tyr Ser Ala Leu Leu Thr Lys Thr Asn Arg
 645 650 655

Ile Ala Arg Ile Phe Gly Gly Ala Arg Glu Gly Ala Gln Arg Pro Arg
 660 665 670

Phe Ile Ser Pro Ala Ser Gln Val Ala Ile Cys Leu Ala Leu Ile Ser
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Gly Gln Leu Leu Ile Val Val Ala Trp Leu Val Val Glu Ala Pro Gly
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Thr Gly Lys Glu Thr Ala Pro Glu Arg Arg Glu Val Val Thr Leu Arg
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Cys Asn His Arg Asp Ala Ser Met Leu Gly Ser Leu Ala Tyr Asn Val
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63

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<400> 39

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Ser Gln Glu Tyr Ala His Ser Ile Arg Val Asp Gly Asp Ile Ile Leu
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Gly Gly Leu Phe Pro Val His Ala Lys Gly Glu Arg Gly Val Pro Cys
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67

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 Thr Leu Gly Val Arg Ile Leu Asp Thr Cys Ser Arg Asp Thr Tyr Ala
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 Leu Glu Gln Ser Leu Thr Phe Val Gln Ala Leu Ile Glu Lys Asp Ala
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 Ile Val Thr Ala Leu Gly Trp Asn Tyr Val Ser Thr Leu Ala Ser Glu
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 Pro Asn Ala Arg Ala Val Ile Met Phe Ala Asn Glu Asp Asp Ile Arg
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 Trp Ile Gly Ser Asp Ser Trp Gly Ser Lys Ile Ala Pro Val Tyr Gln
 305 310 315 320
 Gln Glu Glu Ile Ala Glu Gly Ala Val Thr Ile Leu Pro Lys Arg Ala
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68

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 Cys Lys Leu Gly Ser His Gly Lys Arg Asn Ser His Ile Lys Lys Cys
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 Thr Gly Leu Glu Arg Ile Ala Arg Asp Ser Ser Tyr Glu Gln Glu Gly
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 His Asn Met His Lys Asp Leu Cys Pro Gly Tyr Ile Gly Leu Cys Pro
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 450 455 460
 Gly Asp Ala Pro Gly Arg Tyr Asp Ile Phe Gln Tyr Gln Ile Thr Asn
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 Lys Ser Thr Glu Tyr Lys Val Ile Gly His Trp Thr Asn Gln Leu His
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 Val Lys Gly Val Pro Cys Cys Trp His Cys Glu Arg Cys Glu Gly Tyr
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 Leu Glu Trp His Ser Pro Trp Ala Val Val Pro Val Phe Val Ala Ile
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 Leu Gly Ile Ile Ala Thr Thr Phe Val Ile Val Thr Phe Val Arg Tyr
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 Asn Asp Thr Pro Ile Val Arg Ala Ser Gly Arg Glu Leu Ser Tyr Val
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69

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 Ser Ser Leu Gly Gly Ser Thr Gly Ser Thr Pro Ser Ser Ser Ile Ser
 885 890 895
 Ser Lys Ser Asn Ser Glu Asp Pro Phe Pro Gln Pro Glu Arg Gln Lys
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70

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<400> 41

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Ser	Gln	Glu	Tyr	Ala	His	Ser	Ile	Arg	Val	Asp	Gly	Asp	Ile	Ile	Leu	35	40	45	
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Gly	Glu	Leu	Lys	Lys	Glu	Lys	Gly	Ile	His	Arg	Leu	Glu	Ala	Met	Leu	65	70	75	80
Tyr	Ala	Ile	Asp	Gln	Ile	Asn	Lys	Asp	Pro	Asp	Leu	Leu	Ser	Asn	Ile	85	90	95	
Thr	Leu	Gly	Val	Arg	Ile	Leu	Asp	Thr	Cys	Ser	Arg	Asp	Thr	Tyr	Ala	100	105	110	
Leu	Glu	Gln	Ser	Leu	Thr	Phe	Val	Gln	Ala	Leu	Ile	Glu	Lys	Asp	Ala	115	120	125	
Ser	Asp	Val	Lys	Cys	Ala	Asn	Gly	Asp	Pro	Pro	Ile	Phe	Thr	Lys	Pro	130	135	140	
Asp	Lys	Ile	Ser	Gly	Val	Ile	Gly	Ala	Ala	Ala	Ser	Ser	Val	Ser	Ile	145	150	155	160
Met	Val	Ala	Asn	Ile	Leu	Arg	Leu	Phe	Lys	Ile	Pro	Gln	Ile	Ser	Tyr	165	170	175	
Ala	Ser	Thr	Ala	Pro	Glu	Leu	Ser	Asp	Asn	Thr	Arg	Tyr	Asp	Phe	Phe	180	185	190	
Ser	Arg	Val	Val	Pro	Pro	Asp	Ser	Tyr	Gln	Ala	Gln	Ala	Met	Val	Asp	195	200	205	
Ile	Val	Thr	Ala	Leu	Gly	Trp	Asn	Tyr	Val	Ser	Thr	Leu	Ala	Ser	Glu	210	215	220	

Gly Asn Tyr Gly Glu Ser Gly Val Glu Ala Phe Thr Gln Ile Ser Arg
 225 230 235 240
 Glu Ile Gly Gly Val Cys Ile Ala Gln Ser Gln Lys Ile Pro Arg Glu
 245 250 255
 Pro Arg Pro Gly Glu Phe Glu Lys Ile Ile Lys Arg Leu Leu Glu Thr
 260 265 270
 Pro Asn Ala Arg Ala Val Ile Met Phe Ala Asn Glu Asp Asp Ile Arg
 275 280 285
 Arg Ile Leu Glu Ala Ala Lys Lys Leu Asn Gln Ser Gly His Phe Leu
 290 295 300
 Trp Ile Gly Ser Asp Ser Trp Gly Ser Lys Ile Ala Pro Val Tyr Gln
 305 310 315 320
 Gln Glu Glu Ile Ala Glu Gly Ala Val Thr Ile Leu Pro Lys Arg Ala
 325 330 335
 Ser Ile Asp Gly Phe Asp Arg Tyr Phe Arg Ser Arg Thr Leu Ala Asn
 340 345 350
 Asn Arg Arg Asn Val Trp Phe Ala Glu Phe Trp Glu Glu Asn Phe Gly
 355 360 365
 Cys Lys Leu Gly Ser His Gly Lys Arg Asn Ser His Ile Lys Lys Cys
 370 375 380
 Thr Gly Leu Glu Arg Ile Ala Arg Asp Ser Ser Tyr Glu Gln Glu Gly
 385 390 395 400
 Lys Val Gln Phe Val Ile Asp Ala Val Tyr Ser Met Ala Tyr Ala Leu
 405 410 415
 His Asn Met His Lys Asp Leu Cys Pro Gly Tyr Ile Gly Leu Cys Pro
 420 425 430
 Arg Met Ser Thr Ile Asp Gly Lys Glu Leu Leu Gly Tyr Ile Arg Ala
 435 440 445
 Val Asn Phe Asn Gly Ser Ala Gly Thr Pro Val Thr Phe Asn Glu Asn
 450 455 460
 Gly Asp Ala Pro Gly Arg Tyr Asp Ile Phe Gln Tyr Gln Ile Thr Asn
 465 470 475 480
 Lys Ser Thr Glu Tyr Lys Val Ile Gly His Trp Thr Asn Gln Leu His
 485 490 495
 Leu Lys Val Glu Asp Met Gln Trp Ala His Arg Glu His Thr His Pro
 500 505 510

Ala Ser Val Cys Ser Leu Pro Cys Lys Pro Gly Glu Arg Lys Lys Thr
 515 520 525
 Val Lys Gly Val Pro Cys Cys Trp His Cys Glu Arg Cys Glu Gly Tyr
 530 535 540
 Asn Tyr Gln Val Asp Glu Leu Ser Cys Glu Leu Cys Pro Leu Asp Gln
 545 550 555 560
 Arg Pro Asn Met Asn Arg Thr Gly Cys Gln Leu Ile Pro Ile Ile Lys
 565 570 575
 Leu Glu Trp His Ser Pro Trp Ala Val Val Pro Val Phe Val Ala Ile
 580 585 590
 Leu Gly Ile Ile Ala Thr Thr Phe Val Ile Val Thr Phe Val Arg Tyr
 595 600 605
 Asn Asp Thr Pro Ile Val Arg Ala Ser Gly Arg Glu Leu Ser Tyr Val
 610 615 620
 Leu Leu Thr Gly Ile Phe Leu Cys Tyr Ser Ile Thr Phe Leu Met Ile
 625 630 635 640
 Ala Ala Pro Asp Thr Ile Ile Cys Ser Phe Arg Arg Val Phe Leu Gly
 645 650 655
 Leu Gly Met Cys Phe Ser Tyr Ala Ala Leu Leu Thr Lys Thr Asn Arg
 660 665 670
 Ile His Arg Ile Phe Glu Gln Gly Lys Lys Ser Val Thr Ala Pro Lys
 675 680 685
 Phe Ile Ser Pro Ala Ser Gln Leu Val Ile Thr Phe Ser Leu Ile Ser
 690 695 700
 Val Gln Leu Leu Gly Val Phe Val Trp Phe Val Val Asp Pro Pro His
 705 710 715 720
 Ile Ile Ile Asp Tyr Gly Glu Gln Arg Thr Leu Asp Pro Glu Lys Ala
 725 730 735
 Arg Gly Val Leu Lys Cys Asp Ile Ser Asp Leu Ser Leu Ile Cys Ser
 740 745 750
 Leu Gly Tyr Ser Ile Leu Leu Met Val Thr Cys Thr Val Tyr Ala Ile
 755 760 765
 Lys Thr Arg Gly Val Pro Glu Thr Phe Asn Glu Ala Lys Pro Ile Gly
 770 775 780
 Phe Thr Met Tyr Thr Thr Cys Ile Ile Trp Leu Ala Phe Ile Pro Ile
 785 790 795 800

75

Phe Phe Gly Thr Ala Gln Ser Ala Glu Lys Met Tyr Ile Gln Thr Thr
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 Thr Leu Thr Val Ser Met Ser Leu Ser Ala Ser Val Ser Leu Gly Met
 820 825 830
 Leu Tyr Met Pro Lys Val Tyr Ile Ile Ile Phe His Pro Glu Gln Asn
 835 840 845
 Thr Ile Glu Glu Val Arg Cys Ser Thr Ala Ala His Ala Phe Lys Val
 850 855 860
 Ala Ala Arg Ala Thr Leu Arg Arg Ser Asn Val Ser Arg Lys Arg Ser
 865 870 875 880
 Ser Ser Leu Gly Gly Ser Thr Gly Ser Thr Pro Ser Ser Ser Ile Ser
 885 890 895
 Ser Lys Ser Asn Ser Glu Asp Pro Phe Pro Gln Pro Glu Arg Gln Lys
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 Gln Gln Gln Pro Leu Ala Leu Thr Gln Gln Glu Gln Gln Gln Gln Pro
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 Leu Thr Leu Pro Gln Gln Gln Arg Ser Gln Gln Gln Pro Arg Cys Lys
 930 935 940
 Gln Lys Val Ile Phe Gly Ser Gly Thr Val Thr Phe Ser Leu Ser Phe
 945 950 955 960
 Asp Glu Pro Gln Lys Asn Ala Met Ala His Gly Asn Ser Thr His Gln
 965 970 975
 Asn Ser Leu Glu Ala Gln Lys Ser Ser Asp Thr Leu Thr Arg His Gln
 980 985 990
 Pro Leu Leu Pro Leu Gln Cys Gly Glu Thr Asp Leu Asp Leu Thr Val
 995 1000 1005
 Gln Glu Thr Gly Leu Gln Gly Pro Val Gly Gly Asp Gln Arg Pro Glu
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 Val Glu Asp Pro Glu Glu Leu Ser Pro Ala Leu Val Val Ser Ser Ser
 1025 1030 1035 1040
 Gln Ser Phe Val Ile Ser Gly Gly Gly Ser Thr Val Thr Glu Asn Val
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 Glu Ala Lys Glu Ala Arg Arg Ile Asn Asp Glu Ile Glu Arg Gln Leu
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Arg Arg Asp Lys Arg Asp Ala Arg Arg Glu Leu Lys Leu Leu Leu Leu
 1090 1095 1100
 Gly Thr Gly Glu Ser Gly Lys Ser Thr Phe Ile Lys Gln Met Arg Ile
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 1125 1130 1135
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 Met Asp Thr Leu Lys Ile Pro Tyr Lys Tyr Glu His Asn Lys Ala His
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 Ala Gln Leu Val Arg Glu Val Asp Val Glu Lys Val Ser Ala Phe Glu
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 Asn Pro Tyr Val Asp Ala Ile Lys Ser Leu Trp Asn Asp Pro Gly Ile
 1185 1190 1195 1200
 Gln Glu Cys Tyr Asp Arg Arg Arg Glu Tyr Gln Leu Ser Asp Ser Thr
 1205 1210 1215
 Lys Tyr Tyr Leu Asn Asp Leu Asp Arg Val Ala Asp Pro Ala Tyr Leu
 1220 1225 1230
 Pro Thr Gln Gln Asp Val Leu Arg Val Arg Val Pro Thr Thr Gly Ile
 1235 1240 1245
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 1250 1255 1260
 Val Gly Gly Gln Arg Ser Glu Arg Arg Lys Trp Ile His Cys Phe Glu
 1265 1270 1275 1280
 Asn Val Thr Ser Ile Met Phe Leu Val Ala Leu Ser Glu Tyr Asp Gln
 1285 1290 1295
 Val Leu Val Glu Ser Asp Asn Glu Asn Arg Met Glu Glu Ser Lys Ala
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 Leu Phe Arg Thr Ile Ile Thr Tyr Pro Trp Phe Gln Asn Ser Ser Val
 1315 1320 1325
 Ile Leu Phe Leu Asn Lys Lys Asp Leu Leu Glu Glu Lys Ile Met Tyr
 1330 1335 1340
 Ser His Leu Val Asp Tyr Phe Pro Glu Tyr Asp Gly Pro Gln Arg Asp
 1345 1350 1355 1360
 Ala Gln Ala Ala Arg Glu Phe Ile Leu Lys Met Phe Val Asp Leu Asn
 1365 1370 1375

Pro Asp Ser Asp Lys Ile Ile Tyr Ser His Phe Thr Cys Ala Thr Asp
 1380 1385 1390

Thr Glu Asn Ile Arg Phe Val Phe Ala Ala Val Lys Asp Thr Ile Leu
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Gln Leu Asn Leu Lys Asp Cys Gly Leu Phe
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<210> 42
 <211> 3909
 <212> DNA
 <213> Artificial Sequence

 <220>
 <223> Chimeric GABA-BR2*Gqo5

 <400> 42

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ctcatgccgc	tcaccaagga	ggtggccaag	ggcagcatcg	ggcgcggtgt	gtccccgcgc	240
gtggaactgg	ccatcgagca	gatccgcaac	gagtcactcc	tgcgccctta	cttcctcgac	300
ctgcggctct	atgacacgga	gtgcgacaac	gcaaaagggt	tgaaagcctt	ctacgatgca	360
ataaaatacg	ggccgaacca	cttgatgggt	tttggaggcg	tctgtccatc	cgtcacatcc	420
atcattgcag	agtcctctca	aggctggaat	ctggtgcagc	tttcttttgc	tgcaaccacg	480
cctgttctag	ccgataagaa	aaaataccct	tatttcttcc	ggaccgtccc	atcagacaat	540
gcggtgaatc	cagccattct	gaagtgtgtc	aagcactacc	agtgggaagcg	cgtgggcacg	600
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cgctgcctcc	ggaagaatct	gcttgctgcc	atggagggct	acattggcgt	ggatttcgag	960
cccctgagct	ccaagcagat	caagaccatc	tcaggaaaaga	ctccacagca	gtatgagaga	1020
gagtacaaca	acaagcggtc	aggcgtgggg	cccagcaagt	tccacgggta	cgcctacgat	1080
ggcatctggg	tcacgccaac	gacactgcag	agggccatgg	agacactgca	tgccagcagc	1140
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aatgccatga	acgagacca	cttcttcggg	gtcacgggtc	aagttgtatt	ccggaatggg	1260
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atccgccctc	tcctggagca	ctgtgagaac	acccatatga	ccatctggct	tggtcatcgtc	1980
tatgcctaca	agggaactct	catgttgttc	ggttgtttct	tagcttgagg	gaccgcgaac	2040


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aaccagaca gtgacaaaat taactactcc cacttcacgt gcgccacaga caccgagaat 3840
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<210> 43
 <211> 1303
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Chimeric GABA-BR2*Gqo5

<400> 43

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Pro Pro Pro Pro Ala Arg Leu Leu Leu Leu Leu Leu Leu Pro Leu Leu
          20             25             30

Leu Pro Leu Ala Pro Gly Ala Trp Gly Trp Ala Arg Gly Ala Pro Arg
          35             40             45

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79

Pro Pro Pro Ser Ser Pro Pro Leu Ser Ile Met Gly Leu Met Pro Leu
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 Thr Lys Glu Val Ala Lys Gly Ser Ile Gly Arg Gly Val Leu Pro Ala
 65 70 75 80
 Val Glu Leu Ala Ile Glu Gln Ile Arg Asn Glu Ser Leu Leu Arg Pro
 85 90 95
 Tyr Phe Leu Asp Leu Arg Leu Tyr Asp Thr Glu Cys Asp Asn Ala Lys
 100 105 110
 Gly Leu Lys Ala Phe Tyr Asp Ala Ile Lys Tyr Gly Pro Asn His Leu
 115 120 125
 Met Val Phe Gly Gly Val Cys Pro Ser Val Thr Ser Ile Ile Ala Glu
 130 135 140
 Ser Leu Gln Gly Trp Asn Leu Val Gln Leu Ser Phe Ala Ala Thr Thr
 145 150 155 160
 Pro Val Leu Ala Asp Lys Lys Lys Tyr Pro Tyr Phe Phe Arg Thr Val
 165 170 175
 Pro Ser Asp Asn Ala Val Asn Pro Ala Ile Leu Lys Leu Leu Lys His
 180 185 190
 Tyr Gln Trp Lys Arg Val Gly Thr Leu Thr Gln Asp Val Gln Arg Phe
 195 200 205
 Ser Glu Val Arg Asn Asp Leu Thr Gly Val Leu Tyr Gly Glu Asp Ile
 210 215 220
 Glu Ile Ser Asp Thr Glu Ser Phe Ser Asn Asp Pro Cys Thr Ser Val
 225 230 235 240
 Lys Lys Leu Lys Gly Asn Asp Val Arg Ile Ile Leu Gly Gln Phe Asp
 245 250 255
 Gln Asn Met Ala Ala Lys Val Phe Cys Cys Ala Tyr Glu Glu Asn Met
 260 265 270
 Tyr Gly Ser Lys Tyr Gln Trp Ile Ile Pro Gly Trp Tyr Glu Pro Ser
 275 280 285
 Trp Trp Glu Gln Val His Thr Glu Ala Asn Ser Ser Arg Cys Leu Arg
 290 295 300
 Lys Asn Leu Leu Ala Ala Met Glu Gly Tyr Ile Gly Val Asp Phe Glu
 305 310 315 320
 Pro Leu Ser Ser Lys Gln Ile Lys Thr Ile Ser Gly Lys Thr Pro Gln
 325 330 335

Gln Tyr Glu Arg Glu Tyr Asn Asn Lys Arg Ser Gly Val Gly Pro Ser
 340 345 350
 Lys Phe His Gly Tyr Ala Tyr Asp Gly Ile Trp Val Ile Ala Lys Thr
 355 360 365
 Leu Gln Arg Ala Met Glu Thr Leu His Ala Ser Ser Arg His Gln Arg
 370 375 380
 Ile Gln Asp Phe Asn Tyr Thr Asp His Thr Leu Gly Arg Ile Ile Leu
 385 390 395 400
 Asn Ala Met Asn Glu Thr Asn Phe Phe Gly Val Thr Gly Gln Val Val
 405 410 415
 Phe Arg Asn Gly Glu Arg Met Gly Thr Ile Lys Phe Thr Gln Phe Gln
 420 425 430
 Asp Ser Arg Glu Val Lys Val Gly Glu Tyr Asn Ala Val Ala Asp Thr
 435 440 445
 Leu Glu Ile Ile Asn Asp Thr Ile Arg Phe Gln Gly Ser Glu Pro Pro
 450 455 460
 Lys Asp Lys Thr Ile Ile Leu Glu Gln Leu Arg Lys Ile Ser Leu Pro
 465 470 475 480
 Leu Tyr Ser Ile Leu Ser Ala Leu Thr Ile Leu Gly Met Ile Met Ala
 485 490 495
 Ser Ala Phe Leu Phe Phe Asn Ile Lys Asn Arg Asn Gln Lys Leu Ile
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 Lys Met Ser Ser Pro Tyr Met Asn Asn Leu Ile Ile Leu Gly Gly Met
 515 520 525
 Leu Ser Tyr Ala Ser Ile Phe Leu Phe Gly Leu Asp Gly Ser Phe Val
 530 535 540
 Ser Glu Lys Thr Phe Glu Thr Leu Cys Thr Val Arg Thr Trp Ile Leu
 545 550 555 560
 Thr Val Gly Tyr Thr Thr Ala Phe Gly Ala Met Phe Ala Lys Thr Trp
 565 570 575
 Arg Val His Ala Ile Phe Lys Asn Val Lys Met Lys Lys Lys Ile Ile
 580 585 590
 Lys Asp Gln Lys Leu Leu Val Ile Val Gly Gly Met Leu Leu Ile Asp
 595 600 605
 Leu Cys Ile Leu Ile Cys Trp Gln Ala Val Asp Pro Leu Arg Arg Thr
 610 615 620

81

Val	Glu	Lys	Tyr	Ser	Met	Glu	Pro	Asp	Pro	Ala	Gly	Arg	Asp	Ile	Ser	625	630	635	640
Ile	Arg	Pro	Leu	Leu	Glu	His	Cys	Glu	Asn	Thr	His	Met	Thr	Ile	Trp	645	650	655	
Leu	Gly	Ile	Val	Tyr	Ala	Tyr	Lys	Gly	Leu	Leu	Met	Leu	Phe	Gly	Cys	660	665	670	
Phe	Leu	Ala	Trp	Glu	Thr	Arg	Asn	Val	Ser	Ile	Pro	Ala	Leu	Asn	Asp	675	680	685	
Ser	Lys	Tyr	Ile	Gly	Met	Ser	Val	Tyr	Asn	Val	Gly	Ile	Met	Cys	Ile	690	695	700	
Ile	Gly	Ala	Ala	Val	Ser	Phe	Leu	Thr	Arg	Asp	Gln	Pro	Asn	Val	Gln	705	710	715	720
Phe	Cys	Ile	Val	Ala	Leu	Val	Ile	Ile	Phe	Cys	Ser	Thr	Ile	Thr	Leu	725	730	735	
Cys	Leu	Val	Phe	Val	Pro	Lys	Leu	Ile	Thr	Leu	Arg	Thr	Asn	Pro	Asp	740	745	750	
Ala	Ala	Thr	Gln	Asn	Arg	Arg	Phe	Gln	Phe	Thr	Gln	Asn	Gln	Lys	Lys	755	760	765	
Glu	Asp	Ser	Lys	Thr	Ser	Thr	Ser	Val	Thr	Ser	Val	Asn	Gln	Ala	Ser	770	775	780	
Thr	Ser	Arg	Leu	Glu	Gly	Leu	Gln	Ser	Glu	Asn	His	Arg	Leu	Arg	Met	785	790	795	800
Lys	Ile	Thr	Glu	Leu	Asp	Lys	Asp	Leu	Glu	Glu	Val	Thr	Met	Gln	Leu	805	810	815	
Gln	Asp	Thr	Pro	Glu	Lys	Thr	Thr	Tyr	Ile	Lys	Gln	Asn	His	Tyr	Gln	820	825	830	
Glu	Leu	Asn	Asp	Ile	Leu	Asn	Leu	Gly	Asn	Phe	Thr	Glu	Ser	Thr	Asp	835	840	845	
Gly	Gly	Lys	Ala	Ile	Leu	Lys	Asn	His	Leu	Asp	Gln	Asn	Pro	Gln	Leu	850	855	860	
Gln	Trp	Asn	Thr	Thr	Glu	Pro	Ser	Arg	Thr	Cys	Lys	Asp	Pro	Ile	Glu	865	870	875	880
Asp	Ile	Asn	Ser	Pro	Glu	His	Ile	Gln	Arg	Arg	Leu	Ser	Leu	Gln	Leu	885	890	895	
Pro	Ile	Leu	His	His	Ala	Tyr	Leu	Pro	Ser	Ile	Gly	Gly	Val	Asp	Ala	900	905	910	

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 His Val Pro Pro Ser Phe Arg Val Met Val Ser Gly Leu Ala Ala Ala
 930 935 940
 Met Thr Leu Glu Ser Ile Met Ala Cys Cys Leu Ser Glu Glu Ala Lys
 945 950 955 960
 Glu Ala Arg Arg Ile Asn Asp Glu Ile Glu Arg Gln Leu Arg Arg Asp
 965 970 975
 Lys Arg Asp Ala Arg Arg Glu Leu Lys Leu Leu Leu Leu Gly Thr Gly
 980 985 990
 Glu Ser Gly Lys Ser Thr Phe Ile Lys Gln Met Arg Ile Ile His Gly
 995 1000 1005
 Ser Gly Tyr Ser Asp Glu Asp Lys Arg Gly Phe Thr Lys Leu Val Tyr
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 1025 1030 1035 1040
 Leu Lys Ile Pro Tyr Lys Tyr Glu His Asn Lys Ala His Ala Gln Leu
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 Pro Phe Asp Leu Gln Ser Val Ile Phe Arg Met Val Asp Val Gly Gly
 1140 1145 1150
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 1155 1160 1165
 Ser Ile Met Phe Leu Val Ala Leu Ser Glu Tyr Asp Gln Val Leu Val
 1170 1175 1180
 Glu Ser Asp Asn Glu Asn Arg Met Glu Glu Ser Lys Ala Leu Phe Arg
 1185 1190 1195 1200

Thr Ile Ile Thr Tyr Pro Trp Phe Gln Asn Ser Ser Val Ile Leu Phe
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Leu Asn Lys Lys Asp Leu Leu Glu Glu Lys Ile Met Tyr Ser His Leu
1220 1225 1230

Val Asp Tyr Phe Pro Glu Tyr Asp Gly Pro Gln Arg Asp Ala Gln Ala
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Ala Arg Glu Phe Ile Leu Lys Met Phe Val Asp Leu Asn Pro Asp Ser
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Asp Lys Ile Asn Tyr Ser His Phe Thr Cys Ala Thr Asp Thr Glu Asn
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Leu Lys Gly Cys Gly Leu Tyr
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<211> 3969

<212> DNA

<213> Artificial Sequence

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<223> Chimeric GABA-BR1a*Gqo5

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Tyr Val Cys Arg Gly Glu Arg Glu Val Val Gly Pro Lys Val Arg Lys
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<213> Artificial Sequence

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Val Leu Gly Gly Leu Phe Pro Val His Gln Lys Gly Gly Pro Ala Glu
35           40           45

Asp Cys Gly Pro Val Asn Glu His Arg Gly Ile Gln Arg Leu Glu Ala
50           55           60

Met Leu Phe Ala Leu Asp Arg Ile Asn Arg Asp Pro His Leu Leu Pro
65           70           75           80

Gly Val Arg Leu Gly Ala His Ile Leu Asp Ser Cys Ser Lys Asp Thr
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His Ala Leu Glu Gln Ala Leu Asp Phe Val Arg Ala Ser Leu Ser Arg
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INTERNATIONAL SEARCH REPORT

International Application No.

PCT/US 99/07333

A. CLASSIFICATION OF SUBJECT MATTER
IPC 6 C07K14/705 C12N15/12 C12N15/62 A61K38/17

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 6 C12N

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	WO 97 05252 A (NPS PHARMA INC) 13 February 1997 (1997-02-13) cited in the application see the whole document and specially pages 59-60.	13-28, 33,38,40
Y	WO 97 46675 A (NOVARTIS AG) 11 December 1997 (1997-12-11) cited in the application page 2, last paragraph - page 3, paragraph 1 page 50-56 page 62-67 page 86-90	13-28, 33,38,39

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

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- "O" document referring to an oral disclosure, use, exhibition or other means
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- "T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
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Date of the actual completion of the international search

13 September 1999

Date of mailing of the international search report

28/09/1999

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INTERNATIONAL SEARCH REPORT

International Application No
PCT/US 99/07333

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	KAUPMANN K ET AL: "EXPRESSION CLONING OF GABAB RECEPTORS UNCOVERS SIMILARITY TO METABOTROPIC GLUTAMATE RECEPTORS" NATURE, vol. 386, no. 6622, 20 March 1997 (1997-03-20), pages 239-246, XP002032306 ISSN: 0028-0836 see the whole document and specially Fig.3 ---	13-28, 33
Y	WO 97 48724 A (NPS PHARMA INC) 24 December 1997 (1997-12-24) cited in the application figure 1 ---	13-28, 33, 38, 40
Y	EP 0 816 498 A (LILLY CO ELI) 7 January 1998 (1998-01-07) abstract page 21, line 35-58 page 46-48 ---	13-28, 33, 38, 39
X	WO 97 48820 A (AURORA BIOSCIENCES CORP) 24 December 1997 (1997-12-24) page 3, line 1-4 page 46-53 ---	5, 32
A	WO 92 05244 A (UNIV DUKE) 2 April 1992 (1992-04-02) page 2, line 15-25 page 4, line 20-34 page 10, line 25-36; examples 4, 5 ---	1, 5, 8-10
A	B. BERTIN ET AL., : "Cellular signaling by agonist-activated receptor/Gsalpha fusion protein" PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES, vol. 91, 1994, pages 8827-8831, XP002114989 cited in the application the whole document ---	1, 5, 8-10
A	A. WISE AND G. MILLIGAN : "Rescue of functional interactions between the alpha2A-adrenoreceptor and acylation-resistant forms of Gialpha by expressing the proteins from chimeric open reading frames" JOURNAL OF BIOLOGICAL CHEMISTRY, vol. 272, no. 39, 1997, pages 24673-24678, XP002114990 cited in the application abstract page 24676, paragraph 3 ---	1, 38-40

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INTERNATIONAL SEARCH REPORT

International Application No

PCT/US 99/07333

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
E	<p>WO 99 20751 A (BOROWSKY BETH ; JONES KENNETH A (US); LAZ THOMAS M (US); SYNAPTIC P) 29 April 1999 (1999-04-29) abstract page 105-109; table 3 figures 2A-D</p> <p>-----</p>	<p>13-28, 38, 39</p>

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/US 99/07333

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WO 9705252	A	13-02-1997	AU 6602296 A CA 2200606 A EP 0783577 A JP 10507934 T	26-02-1997 13-02-1997 16-07-1997 04-08-1998
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